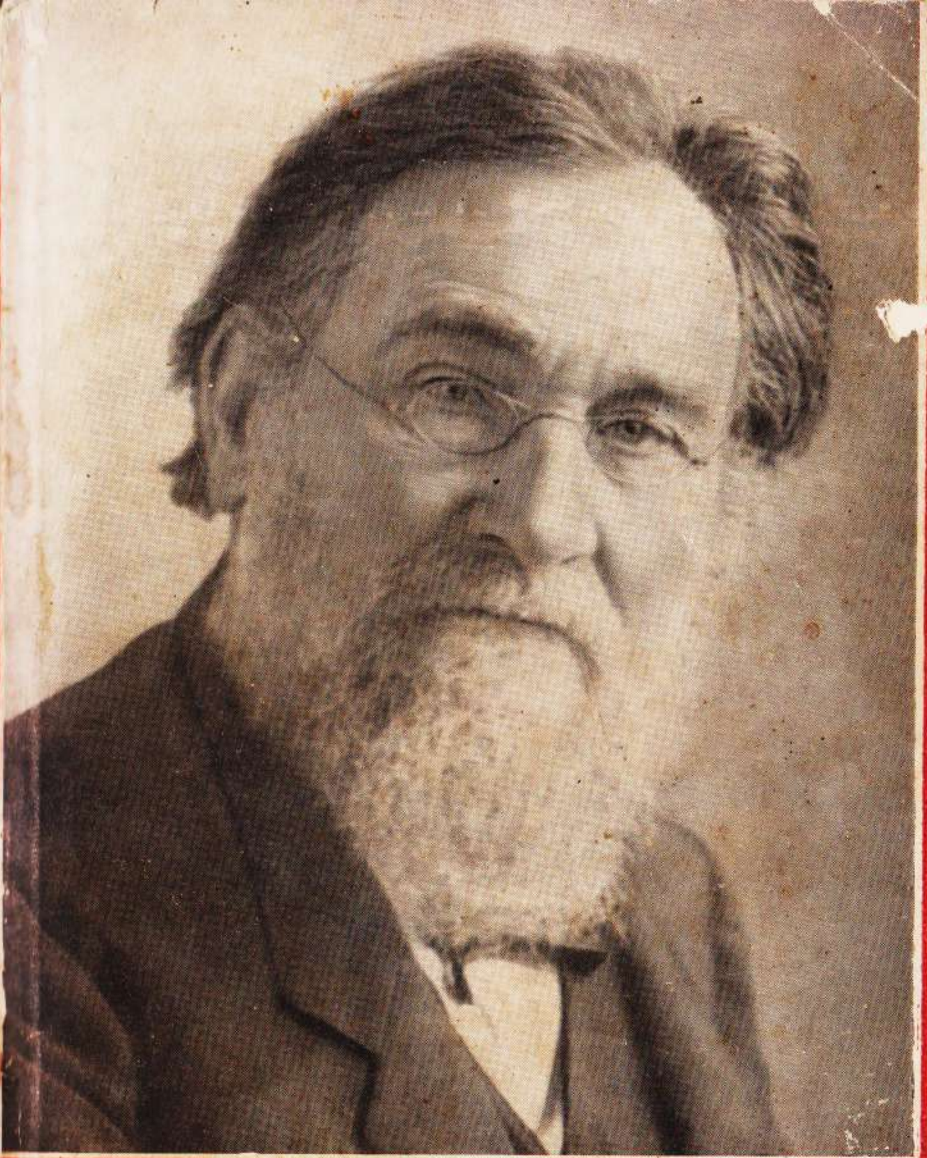

S. ZALKIND

ILYA MECHNIKOV

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Prof. Semyon Zalkind

ILYA MECHNIKOV

HIS LIFE AND WORK

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ИЛЬЯ МЕЧНИКОВ
Жизнь и творческий путь

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FOREWORD

Mechnikov is one of those famous Russian scientists who, like Mendeleyev, Butlerov, Sechenov, Pavlov, the Kovalevsky brothers, and Timiryazev, are the pride of Russian science—having won for it an honourable place in world science. Odessa University, where Mechnikov was at his best as a professor, bears his name, as do many research medical and biological institutions in Moscow, Kharkov and other cities of the Soviet Union. The U.S.S.R. Academy of Sciences yearly awards the Mechnikov Prize and a gold medal for the best works in the fields of science associated with his name.

Much has been written about Mechnikov, the best biographical works being the one written by Olga Mechnikova, his wife and devoted friend, and the reminiscences of his colleagues and pupils, A. Bezredka, N. Chistovich and L. Tarasevich. The academic collection of Mechnikov's works is supplemented by numerous commentaries and notes written by well-qualified specialists. *Pages of Reminiscences*, a small but very important collection of Mechnikov's articles and letters, was published in 1946. Lectures on Mechnikov are published every year; there are even books for children portraying the life of this great scientist. And yet in spite of the abundance of literature on Mechnikov, those who revere him as a scientist and man cannot help but feel a certain amount of dissatisfaction. This dissatisfaction is due chiefly to the fragmentary nature of the material available about him—his personality is so multi-faceted that no single work can embrace it in all of its aspects. That is perhaps why each author deals only with that part of Mechnikov's work which is familiar to him—be it embryology, microbiology, pathology, or the advocacy of orthobiosis. And although a selection of interests and themes is quite justifiable, it is, nevertheless, fraught with the danger of destroying the unity of Mechnikov's personality, of splitting it into the minutiae of biographical details.

Yet another reason for the feeling of dissatisfaction which arises in the study of Mechnikoviana is the extreme difficulty in portraying Mechnikov the man. His was a very complex and contradictory personality. Only a careful analysis of facts, casual remarks, and events recollected by people who met him, permits the creation of a true portrait. Then Mechnikov arises before one's eyes as a very winning personality. Unfortunately, many of his biographers have failed in fulfilling their task.

Last but not least, we of the older generation, i.e., those born at the beginning of the present century, regard Mechnikov as a contemporary. It will suffice to mention his influence upon the youth in those years—Russia oppressed by an outmoded regime, ridden by the arbitrary and wild rule of a Ministry of Public Education under Kasso; clouds of powder smoke rising from the Balkans, blood and suffering resulting from the World War. Many young people who had no clear political perspective were assailed by pessimism, a serious disease of the times further complicated by the general hapless situation. Against this sombre background, what a ray of hope, what boundless faith in the triumph of science were Mechnikov's books, such as *The Nature of Man*, *Studies in Optimism*, and *Forty Years' Search for a Rational Outlook*! On reading them, one wanted to live, to fight, to learn—in order to emulate him, that bearded campaigner against disease and old age.

Professor N. Chistovich has very aptly said: "Mechnikov cured us of disappointment," a serious affliction in those days, as I have already indicated. Mechnikov himself had traversed the hard road from pessimism to optimism, from excessive sensibility to wise stoicism and he was able to lead the turbulent, seeking Russian student youth of the pre-revolutionary years along that same path. The initial impact of Mechnikov's personality on a fresh, youthful mind persists throughout life, giving birth to a feeling of immense gratitude for his timely assistance and to a sensation of warmth occasioned by a personal encounter with a great and extremely humane man. I should like to portray Mechnikov the man, the thinker, the fighter, as we knew him when we were young.

The above considerations have encouraged me in my attempt to delineate the personality and career of this great Russian biologist.

INTRODUCTION

December 1882. It is warm and sunny on the Mediterranean at this time of year. In a small house in Messina, Ilya Ilyich Mechnikov, a Russian zoologist, lives with his family. Although he is not yet forty, he is well known in Russia and abroad; he is the author of numerous exhaustive investigations of the development of invertebrates; he is a professor at Odessa University, a favourite with the students.

Mechnikov is bent over a microscope, looking intently at a transparent starfish larva—he is studying the process of intracellular digestion. Minute dark objects—grains of India ink—have been introduced into the body of the larva. Curiously-shaped iridescent wandering cells are seen to move towards the grains from all directions, to envelop and swallow them. Soon the larva's body is freed from the foreign (and probably harmful) particles. As Mechnikov follows the events developing before him, a new idea grasps his mind; he rushes into the garden, picks some thorns from a rosebush and thrusts them under the skin of the larva. He has started an experiment that will either confirm or nullify his daring idea. After a restless night, early in the morning, Mechnikov hurries to his microscope. His conjecture is correct: the "splinter" in the larva's body is surrounded by a host of wandering cells—amoebocytes.

* * *

In this way, an idea was born and experimentally proved—Mechnikov's brilliant idea that wandering cells occurring in large numbers throughout the animal kingdom, from simple multicellular organisms to man, are the chief elements of defence of various organisms. Phagocytosis—the envelopment and subsequent ingestion of extraneous matter—indicates the ability of an organism to combat pathogens, especially bacteria.

The "Messina incident" is highly characteristic of Mechnikov, who had a remarkable ability to integrate seemingly disconnected facts into a unified whole. Prior to Mechnikov, many zoologists had studied the structure of invertebrate embryos and many pathologists had known and described in detail the processes occurring in a living organism when a foreign body penetrates it, but Mechnikov's insight and perspicacity enabled him to uncover in these separate, disconnected facts an idea. With the help of this idea, he was able to throw light on phenomena hitherto incomprehensible, thus opening to study a new, very important sphere of investigation.

This example is by no means exceptional. Mechnikov's career abounds in flights of inspiration, in the surmises and inferences of a genius. He had the qualities (shared by few of his contemporaries) that make a man great—a passion for truth and the fiery temperament of a fighter. The "Messina incident" which Mechnikov himself recalled with such warmth many years later (in 1912), proved to be a turning-point in his life. From that time on, his scientific interests changed and zoologist Mechnikov became a pathologist devoting the rest of his life to problems of theoretical medicine.

Unlike many scientists who pursue the study of one science without any deviation, Mechnikov pursued a path which crossed many sciences, paying close attention to new spheres of learning, and passing from one scientific discipline to another. Though highly unusual, this creative evolution was, nevertheless, perfectly natural. And it is but natural that in order to understand Mechnikov the man and the scientist, one must follow, step by step, all the stages of his extraordinary life.

CHILDHOOD, YOUTH AND FIRST WORKS

Ilya Ilyich Mechnikov was born on May 3 (16 New Style), 1845, in the village of Panasovka, Kupyansk District, Kharkov Gubernia, into the family of a small landowner. Ilya Ivanovich Mechnikov, his father, had served in the Guards, but lack of sufficient means forced him to retire and settle on his estate where he devoted himself to agriculture, evidently with but little success. He did not exert any appreciable influence on the spiritual development of his children. His wife, Emilia Lvovna, *née* Nevakhovich, was a very accomplished woman, possessed of a warm heart. She bent all her energies towards educating her children. Ilya Mechnikov always remembered his mother with the utmost tenderness and profound gratitude for the atmosphere of moral purity and uprightness, understanding and benevolence which she established in the family. As future events proved, the family was not an ordinary one. Ivan, the eldest son, became a prominent lawyer. Another brother, Lev, a noted geographer and traveller, lived abroad because of his revolutionary convictions and was Garibaldi's adjutant and close friend. In his memoirs, Herzen speaks of Lev Mechnikov with great respect.

Ilya, however, was the most talented member of this gifted family. While yet a small boy, he displayed unusual vivacity and brilliant abilities. These qualities ensured an exceptionally early mental development. His first critical article was published when Mechnikov was sixteen and his first scientific work, "Some Facts from the Life of Infusoria," was done when he was eighteen years old. At the age of nineteen, he graduated from Kharkov University, having finished the entire course given by the natural science department in two years. At twenty-two, he received his master's degree in zoology and became a docent at Novorossiisky (Odessa) University. Mechnikov presented his Doctor of Zoology thesis when he was twenty-three and was elected professor at that university at the age of twenty-five. According to his brother, Nikolai, little Ilya had paid his brothers and sister two kopeks each for listening to what he termed "lectures on scientific subjects." Olga Mechnikova (his wife) recalls that, when he was a sixth-form pupil, Mechnikov was very much interested in zoology and applied to Maslovsky, a professor at Kharkov University, "to be allowed to study protoplasm under his guidance." The professor, however, refused point-blank and advised him to finish school first and then enter the university. Mechnikov was so offended by this reply that, when he became a student at the university, he refused to work under Maslovsky in spite of common scientific interests.

At a maturer age, Mechnikov was more tolerant of those who offended him. When, for example, he perceived that Koch treated him and his ideas with hostility, he harboured no ill feelings, often asserted Koch's merits publicly and named him as a candidate for the Nobel Prize. Toward the end of his life Koch admitted that Mechnikov had been right in many of his assertions, and the two scientists became close friends.

* * *

Mechnikov delineated for himself at a very early age the sphere of his interests in biology. Khodunov, a medical student who lived with the Mechnikovs as a tutor, persuaded him to keep a herbarium when Ilya was eight, and, at eleven, he studied the life of the hydra. At the age of

fifteen, after reading H. G. Bronn's *Classes and Orders of the Animal Kingdom*, translated by A. Bogdanov, a well-known zoologist, Mechnikov "decided to devote his attention to the study of the lowest among the animal kingdom, the manifestation of life in its simplest form," as his biographer, Olga Mechnikova, says.

Did Mechnikov choose his speciality by chance? We think that the answer is "No."

Mechnikov passed his boyhood during the years that possessed special significance for the history of Russian society—the celebrated sixties. What those years meant for the Russian intelligentsia can be seen from the following vivid description of Kliment Timiryazev: "The generation, the beginning of whose conscious existence coincided with what is commonly termed 'the sixties,' was doubtlessly the happiest of any born in Russia. The spring of the personal life of this generation was at one with the common spring and its breath which swept over the entire country, awakening it from its mental sleep and stagnation that had held it bound for over a quarter of a century." This is what he says about the impetuous movement of contemporary youth: "If we should be asked what the salient feature of this movement was, we would answer unhesitatingly in a word: enthusiasm."* And this is what Mechnikov himself says about the second half of the sixties in his *History of Biology in Russia* (1913): "Fifty years ago . . . society was in a ferment and experienced a resurgence in mental activity. The scientific aspirations of secondary-school pupils were encouraged, not suppressed by too strict demands on their classical education. Greek was absent from the curriculum and Latin was a mere formality of secondary importance. Their place was taken by natural sciences which attracted special attention of young people. The traditional lectures 'according to the book' in universities were superseded by a livelier presentation of the subjects from scientific sources, and scientists working independently gradually began to make their appearance."

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* K. Timiryazev, *The Development of Natural Science in Russia in the Sixties*, Granat, 1920.

The revolutionary democrats Dobrolyubov, Chernyshevsky and Pisarev reigned supreme in the minds of youth. Progressive student youth adopted the philosophy of materialism. The works of Büchner, Moleschott and Vogt were widely read, in spite of their elementary mechanistic nature. Life called upon the youth to act.

At that time a momentous political differentiation took place among progressive student youth. One section, more public-conscious and far-sighted, devoted themselves unreservedly to political activity, understanding clearly that only a radical change in the political regime of the country could bring about a new life; another section of the youth sought to solve all "accursed problems" of Russian life through enlightenment. Hence their enthusiasm for natural sciences, particularly their practical aspects, such as medicine, agronomy, forestry; hence the "cult" of "positive natural science" so characteristic of the "men of the sixties."

Mechnikov, too, felt the influence of the revolutionary democrats and enlighteners. He and his schoolfellows would gather at Bogomolov's (a student) and read *Polyarnaya Zvezda* (*Polar Star*) and *Kolokol* (*The Bell*),* as well as other forbidden literature brought from abroad. His theme on matriculation, "The Significance of Papal Power in the Middle Ages," is evidence of Mechnikov's broad and deep humanitarian interests. The opinion of specialists was that this work of a schoolboy would do credit to a university student.

And yet Mechnikov's greatest interests lay in the sphere of natural science, which was quite typical of the atmosphere in the Kharkov secondary school, and indeed in other schools as well. Academician V. Zalensky, a fellow-student of Mechnikov's and himself an outstanding zoologist, said: "We found the time to read serious books and scientific works, we wrote essays on particular problems and engaged in disputes." Small wonder that Mechnikov was outstanding among the youthful enthusiasts of science. He was greatly impressed by reading H. T. Buckle's *History of Civilization in England*, in which the author maintained that progress and the happiness of humanity depended on the progress of science. Mechnikov, who always strove to put his convictions into practice, founded in his school a Scientific Union whose members read papers on scientific problems and even attempted to write an encyclopaedia. He himself undertook the difficult task of acquainting the members of the Union with materialist philosophy. He was so taken up with this idea that for some time he neglected his lessons, devoting all of his time to the study of German in order to read Feuerbach in the original. When Mechnikov was in the sixth form, he, together with Zalensky, translated from the French W. R. Grove's *Correlation of Physical Forces*, a book presenting a materialist interpretation of the basic physical laws.

Mechnikov further propagated his materialist views by the advocacy of atheism at school and at home, earning for himself the nickname of Ilya "God-Is-Not." It was probably for his anti-religious views that Mechnikov, who was a good pupil, invariably received a poor grade—4—for conduct (the next lower mark, 3, meant expulsion from school).

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* *Polar Star* was a literary and political symposium published annually (in Russian) from 1855 to 1862 and in 1869 by A. Herzen (after 1858, it was published by Herzen jointly with N. Ogaryov) in the Free Russian Press in London.

Polar Star published Herzen's and Belinsky's articles denouncing serfdom and autocracy in Russia, poems by Pushkin, Ryleyev and Lermontov banned by the censors, and material on the liberation movement in Russia.

The Bell was a revolutionary journal which Herzen and Ogaryov published from 1857 to 1867, first in London and after 1865, in Geneva.—*Ed.*

Natural science became his life's work. Mechnikov brought to it his indomitable spirit as a fighter, the untiring energy of a researcher, a veneration for the miraculous power of science, a naive faith that science and science alone could bring happiness to mankind.

* * *

The first stage in Mechnikov's scientific career was the study of protistology, a branch of zoology. We have no data as to the degree of freedom he enjoyed in the choice of the subject of his first research work. At the same time there is no evidence that anyone supervised Mechnikov's work during that period. Olga Mechnikova states that in the spring of 1862, Mechnikov, then a pupil in the graduating class, made a study of the life of infusoria. These observations were incorporated in his work "Some Facts from the Life of Infusoria," written in the autumn of 1862.

Ilya Mechnikov in 1862 when he finished school

This article suffered a curious fate. When it was ready, Mechnikov sent it to the *Bulletin of the Moscow Society of Explorers of Nature*. The editors accepted it. But, as Olga Mechnikova writes, he soon "discovered that he had drawn erroneous conclusions in mistaking degeneration for reproduction. He at once wrote to the editors asking them to stop the publication of his article. That is how his first work was destined not to see the light of day." Mechnikov was certain that the article had not been published and considered "The Investigation into the Contractile Stem of Infusoria" to be his first published work. And yet the scientist and his wife were both mistaken. The article in question *was* published, although at a later date—in April 1865—without the author's knowledge or consent, as Soviet biologist A. Gaisinovich was able to establish in 1946. And this is how it happened.

The editors of the *Bulletin* referred the article to another publication of the Society, *The Courier of Natural Sciences*, a popular science magazine, the first in Russia, founded in 1854 by K. Rulye, a well-known Russian zoologist. In the course of time, the magazine acquired a more specialized character, lost its subscribers, its issues began to come out belatedly and in 1860, it went out of existence altogether. The subscribers probably objected and the Society of Explorers of Nature was obliged to continue publication of the magazine for the remainder of 1860. I. Auerbach, the Society's secretary, became the editor and was faced with the difficult task of providing material for ten numbers of the magazine which should have appeared in 1860. The issues were published in batches at long intervals, and finally, in April 1865, the last issue appeared. This thick volume was filled with diverse material, a kind of "reserve" at the disposal of the editors. In this way, along with articles translated from foreign languages, letters from members residing in the provinces, minutes of the Society and the like, Mechnikov's article appeared. Mechnikov had requested that the publication of his article be stopped but the manuscript had not been returned to the author. The new editor had no knowledge of the article's "prehistory," and he published it just as he found it, without securing the author's permission. The article, written in October 1862, was thus published in April 1865 in a little-known magazine bearing an 1860 date. No wonder that to the end of his days Mechnikov knew nothing of the publication of his article and that most of his biographers were similarly ignorant.

* * *

What was it like—the first scientific work of a future great biologist? It shows clearly that the author, a first-year university student, was well familiar with the basic literature on Protozoa and adhered to the view that they were unicellular organisms, an opinion which was contested by many eminent scientists, including Claparède and Leydig, who classed them with the Coelenterata. Mechnikov's work consisted of three parts. The first was devoted to the investigation of the contractile vacuole in *Vorticella convallaria*, maintaining that the period of contraction depended on the concentration of the food in solution. In a solution of high concentration, pulsations were observed to be fewer; this coincided with the opinion of some investigators who held that the vacuoles served to excrete water from the cell in order to establish an osmotic balance. May I remind my readers that, today, the dependence of the velocity of pulsation on the concentration of salts in a medium, has been established with certainty, and the excretion of water through the contractile vacuole is acknowledged as the most important factor in osmotic regulation in Protozoa. In the conclusions drawn from his simple experiments, Mechnikov anticipated the results which science obtained at a later date with the aid of considerably more precise methods.

The second part of his work dealt with the reproduction of *Euglena viridis* and described the emergence of the "embryo" from the body of the protozoan. True, Mechnikov worded this conclusion very cautiously· "I cannot be quite certain about it, because my observations failed to establish a genetic connection between *Euglena* and the above-mentioned organisms." We have reason to think that Mechnikov really was in error and had mistaken organisms which were probably parasitic in *Euglena* for *Euglena* embryos.

In the third part of his work, Mechnikov described the separation of a "colourless sack" from the body of the infusoria. What happened to the "sack" after separation,

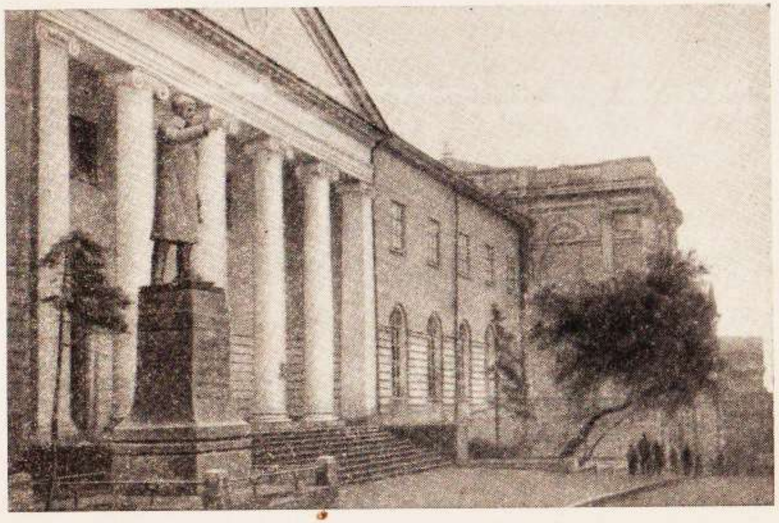
Mechnikov had been unable to discover. It was to this part of his work that Mechnikov subsequently attached his correction in his letter sent to the editors. He rejected his original conjecture that this was a kind of reproduction and substituted a more feasible hypothesis, namely, that the phenomenon he had observed was connected with a process of degeneration. Although the article is rather unfinished and contains insufficient factual material, the observations made by Mechnikov, the schoolboy, (the article was written in his first year at the university) reveal a characteristic feature of Mechnikov the scientist —keenness of observation.

His refusal to have the article published is proof of the youthful author's scientific honesty and courage, for it is not easy for a novice researcher to admit in a letter to a scientific society that he has made a mistake. This incident is very typical of the mature scientist.

* * *

Throughout his short stay at the university (1862-64), Mechnikov maintained his interest in protistology to which he applied himself under the guidance of I. Shchelkov, a young professor of physiology, the great Russian biologist's first instructor. Mechnikov harboured a feeling of profound gratitude towards Shchelkov and wrote of him with appreciation in his *History of Biology in Russia.* Although not an outstanding researcher, Shchelkov was a well-educated biologist and good teacher, capable of inspiring his students with an interest in experimentation and developing in them a will to work. Besides Mechnikov, several of Shchelkov's pupils became noted scientists (one of them was V. Danilevsky, an outstanding Russian physiologist).

The choice of the theme for Mechnikov's second work was determined both by his own interest in protistology and his teacher's who was particularly keen on contractile movements in Protozoa. Thus *Vorticella convallaria* be-



Kharkov University

came, for the second time, the subject of Mechnikov's research. In this work, he sought to verify the data on the nature of the contractile stem of *Vorticella* published by a well-known German researcher, W. Kühne. Apparently Shchelkov was interested in the contractile power of the stem and its similarity to a muscle fibre. The work was published in Vol. 4 of *Transactions of the Academy of Sciences* for 1863 and in German, in Müller's *Archive.* (*Arch. Anat. Physiol, u. wiss. Mediz.*, 1863.)

The most important observation made in this work was that reagents which usually resulted in contraction of muscle tissue did not affect the contractile stem of *Vorticella.* Hence Mechnikov concluded that this organ of the Protozoa had a specific structure and performed specific functions. As the author himself admitted, this work was the effort of a student and contained no important scientific data.

Mechnikov disagreed with Kühne and was bold enough to say so. The German physiologist was offended by the audacity of an unknown Russian youth who had dared to contradict him, a famous man of science. He wrote a harsh, almost rude, article in reply, which, however, did not daunt Mechnikov who persisted in his opinion. A heated controversy was the result.*

This work, unimportant scientifically, showed what a firm and resolute scientist eighteen-year-old Ilya Mechnikov was.

During his university years, Mechnikov completed and published four research themes, two dealing with the contractile stem of *Vorticella,* one on a new genus of *Diplogaster* worms and one on parasitism in Infusoria (about *Sphaerophrya,* parasitic infusoria belonging to the Suctoria). At that time, he worked preponderantly on protistology, but gradually Mechnikov abandoned this particular field and became a zoologist with universal interests, contributing to almost all the branches of invertebrate zoology. Mechnikov fulfilled all curriculum requirements within two years and graduated from Kharkov University in the summer of 1864. He decided to devote his life to science and went abroad to continue his studies.

FIRST PERIOD OF INDEPENDENT RESEARCH. MECHNIKOV'S STAY ABROAD. HIS CONFLICT WITH LEUCKART

Work at an institution, such as Kharkov University was at that time, could not satisfy young Mechnikov who was bubbling with energy. He was eager to study sea animals and work in the laboratory of a great scientist. Having graduated from the university in the summer of 1864, he left for the island of Helgoland which, with its famous biological station, was the Mecca and Medina for young zoologists.

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* Mechnikov was wrong—the contractile stem of *Vorticella* contains contractile elements morphologically and physiologically similar to the non-striated muscle fibres in multicellular organisms.—*Author's note.*

Mechnikov had scant means at his disposal. He wanted the small sum which his parents had saved for him by dint of great effort and strict economy to suffice him for the several months on the island where he was to study Baltic Sea fauna as well as for Giessen where he meant to attend a congress of naturalists and physicians in September. His intention was to present the results of his work on Helgoland to this scientific assembly in a report "On the Sense Organs of Ringworms—the Annelida." His prolonged stay abroad and trip to Giessen required the strictest possible economy and this is what he wrote to his mother on July 31 (August 12), 1864: "In order to realize my dearest wish... I must stay three weeks longer on Helgoland, go to Giessen, live there for ten days and come back on the money which I thought was to last me till the 24th (12th) of August....

"Instead of putting up at a hotel, I hired a room at a fisherman's house at half the price of a hotel. Instead of dining and drinking coffee as heretofore, I eat anything and anywhere, spending not more than 30 kopeks on board; instead of changing my linen twice or three times a week, I change it once or twice. This cuts my laundry expenses. The money saved in this way plus the sum which I have been keeping for settling in St. Petersburg are enough to enable me to derive all the pleasure and benefits I want." Fearing, however, that this frank statement of his affairs might alarm his mother, he went on, "For Goodness' sake, do not think I am complaining or grumbling at my new life; on the contrary, I'm so very happy at knowing how much I am going to profit by all this and at the consciousness of not wantonly wasting the money saved for me with such love and care that I am quite willing to live like this in the future." (Mechnikov's Letter to his Mother, *Pages of Reminiscences*, 1946, p. 154.)

His dearest wish was realized. Mechnikov went to Giessen where he presented two reports at the congress of naturalists and physicians. Mechnikov and T. W. Engelmann, who later became a famous physiologist, were the youngest participants at the congress and attracted the general attention of those present.

Ilya Mechnikov in 1865

* * *

It was not the congress alone that drew Mechnikov to Giessen. Karl Rudolf Leuckart, an outstanding zoologist, the father of modern parasitology, lived and worked there, and Mechnikov was eager to see his wonderful collection as well as work under his guidance.

Leuckart accorded him a cordial welcome and even helped him in obtaining the means for his stay in Giessen.

Nikolai Pirogov, the famous Russian anatomist and surgeon who was living in Berlin at the time, had been commissioned by the Russian Ministry of Public Education to supervise the granting of "professors' scholarships" which were given to young men sent abroad to qualify for professorship. In spite of his brilliant and precocious performance at the university, Mechnikov could not lay formal claim to this scholarship, since a certain Stepanov had been nominated by Kharkov University as a candidate for it. Leuckart, however, wrote in very glowing terms of Mechnikov in his letter to Pirogov and asked that an exception be made in Mechnikov's favour.

Pirogov asked Mechnikov to supply certain data which was to accompany his application. The Archives of the Ministry of Public Education contain Mechnikov's answer, published in 1946. Pirogov accepted Mechnikov's application, and the latter was granted the scholarship (1,600 rubles annually, from January 21, 1865 to March 1867). Mechnikov was now provided for and could devote himself "to zoology at large," as he wrote to Pirogov.

His first study was devoted to roundworms, Nematoda, in which both he and Leuckart were particularly interested at the time. Mechnikov was fortunate in quickly making an important discovery—in studying the life cycle of the nematode *Rabdias* (which was then called *Ascaris nigrovenosa*), he established that free-living and parasitic generations regularly alternated. The former were found in the earth and existed as two separate and distinct sexes. The latter were found in the cloaca of the frog and were hermaphroditic. Each generation reproduced independently. At that time, the phenomenon of alternating generations was a recent discovery and was studied with extreme interest since it served to demonstrate the mechanism of parasitism, that important biological process.

Mechnikov made his discovery on his own and the method he used (placing the larvae in moist earth) was original. He discussed his experiment and its results with his professor. For some time they continued the work together and it was decided that the results would be published in a Russian medical journal over both of their signatures. What then was Mechnikov's astonishment and indignation when he learned by chance that, without saying a word, Leuckart had published the discovery of the alternation of generations in *Ascaris nigrovenosa* in a German journal (*Arch. f. Anat. u. Physiol.* for 1865) over his own signature! Mechnikov's part in the work was characterized, in passing, as "the lively interest Mr. Mechnikov displayed in the observations and experiments of his professor." For the first time, Mechnikov encountered treachery among scientists; for the first time, he was bitterly disappointed in one whom he had deeply respected. Another young scientist might have been defeated, but not Mechnikov, who was confident of being in the right and had the pluck to see the matter through. He sent an article to the very same journal, clarifying the matter. Then Leuckart's reply denying Mechnikov's priority in the discovery was published. Since it was no longer possible to continue an altercation in a scientific magazine, which was assuming more and more of a personal character, Mechnikov took a decisive step. He published, at his own expense (in Göttingen, 1866), a pamphlet in which he explained in detail the unpleasant incident, reflecting but little credit on the name of a famous scientist. Mechnikov provided all the details of that highly unsavoury story: he cited dates and proved that he had made the main discovery during the autumn holidays when

Leuckart had not yet returned to the laboratory. Mechnikov named witnesses (for instance, Evald, a Russian zoologist who was present at an important conversation between Mechnikov and Leuckart) who could disprove some of Leuckart's assertions. He concluded the introductory part of his pamphlet with the following words, "Even if I cannot prove everything I *give my word of honour* that all I have written here is true." (Italics mine.—*S.Z.*) This belief in a "word of honour" on the part of a young man who had just been disabused of the honour of a famous scientist is both singularly naive and extremely touching.

As Mechnikov could no longer remain in Giessen, he went to Göttingen and then to Munich where he worked on a number of interesting problems under the guidance of the well-known scientists Keferstein, Henle and Siebold.

About that time—in the summer of 1865—he visited Naples for the first time and fell under the spell of the Mediterranean, one of the most beautiful of all the seas and abounding in all kinds of marine life. For the rest of his life, or at any rate, for the seventeen years of his "zoologist's life," Mechnikov loved the Mediterranean Sea ardently.

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Among all of Mechnikov's varied interests during the first period of his independent work, problems connected with biology and morphology, or rather with the general aspects of zoology, were the foremost. Parasitology occupied first place—a field in which he made a number of other studies in addition to the one dealing with the alternation of generations in the *Ascaris*. In his early Kharkov years, Mechnikov had studied parasitic infusoria, roundworms and tapeworms. He then observed the evolution of *Gyrodactilus*, a viviparous parasite on fish (infesting their gills). He wrote several works on the morphology of higher worms, on the comparative histology of excretory organs, and on the systematics of animals. In 1866, he described intracellular digestion in *Geodesmus bilineatus* (a ciliary worm)—a very important process of which Mechnikov made use in his subsequent work.

Another interest which made itself felt with increasing persistence about that time was his interest in embryology, one of the oldest and very important branches of zoology. The twenty-one years of Mechnikov's work as zoologist (from 1861 to 1882) were devoted chiefly to embryology.

But before we consider Mechnikov as an embryologist, we should touch upon the events in his life during those years.

MECHNIKOV RETURNS TO RUSSIA. WORK IN ODESSA AND ST. PETERSBURG

When the term for which he was granted the scholarship expired, Mechnikov returned to Russia. In St. Petersburg, at the beginning of 1867, he presented his master's thesis on the "History of the Embryonal Development of Sepiola" (a cephalopod mollusc)—a work which was distinguished by his exhaustive and novel treatment of the material and by the wealth of facts he presented.

Mechnikov's exceptional abilities were recognized and, together with A. Kovalevsky, he was awarded the Baer Prize.* In the same year, Mechnikov, who was then twenty-two years old, was appointed docent in the department of zoology at the newly opened Novorossiisk University in Odessa.

Teaching was a new experience to Mechnikov and although he applied himself to his new duties with enthusiasm, the atmosphere in the department and in the university was hostile. Professor I. Markuzen, who occupied the chair of zoology, was a votary of the old school and a man endowed with excessive self-esteem. From the very beginning, he took a dislike to Mechnikov, probably envying the young scientist's brilliance and European reputation.

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* Karl Baer was a famous Russian zoologist.—*Ed.*

The relations between the two scientists became especially strained in connection with the matter of electing a delegate to the First Congress of Naturalists which was to convene in St. Petersburg at the end of 1867. Both Markuzen and Mechnikov expected to be sent to the congress. Mechnikov was preparing a paper on germ layers for the congress. A conflict ensued—the professors wanted to delegate Markuzen in consideration of his age and experience; the students (who learned the cause of the conflict from Mechnikov himself) openly disapproved of Markuzen and supported the young docent who was very popular with them. The University Council had to compromise by delegating both. Mechnikov left Odessa with a heavy heart. He realized that he had failed to strike firm roots in Odessa and thought of leaving it for ever.

The success with which his report met at the congress enabled Mechnikov to realize a dream he had cherished for some time—to become docent at St. Petersburg University where the chair of zoology was occupied by Karl Kessler, a famous zoologist, very well disposed towards Mechnikov.

Although the university was located in the capital, its zoology department possessed only primitive equipment and the conditions for scientific work were very unsatisfactory. In addition, his interest in embryology was asserting itself; Mechnikov was attracted to the south and felt a need to continue his work on Mediterranean fauna. The university encouraged the young scientist's aspirations and commissioned him to go abroad for the summer vacation in order to proceed with his embryological research.

But there, too, trouble awaited Mechnikov. Indeed, this period of his life can be considered the most difficult.

During his scientific trip to Naples and Messina in the summer of 1868, he suffered the first attack of the eye disease which was later to cause him so much agony; the disease was probably occasioned by overwork. Since he could no longer use the microscope, he was unable to complete his research, which was a severe blow to the impetuous and impatient Mechnikov. It was a tired, exhausted and irritable Mechnikov who returned to St. Petersburg in the autumn. Things had not mended there; as before, the department had no laboratory, the conditions for research were as difficult as ever and in addition, Mechnikov took on some uninteresting work—delivering lectures on zoology at the Mining Institute—in order to have more means at his disposal.

In December of that year Mechnikov took an important step—he married Lyudmila Fedorovich. His choice of a wife was so characteristic of the man that we shall dwell on it in more detail.

A high-strung and nervous person, Mechnikov had a very tender heart and desired the companionship of someone who would be very dear to him, would understand and comfort him. He was so sensitive that the inevitable blows which he sustained in life made a lasting and painful impression on him. On the other hand, he required someone on whom he could lavish his tenderness, attention and care. His mother had long occupied this role, but in the course of time, his thoughts about marriage became more and more pressing.

A day-dreamer, Mechnikov thought he could "create a wife" for himself. He wanted to educate a young girl in accordance with his ideal and then marry her, thus securing a wife and a friend who would share all his joys and sorrows. He chose the thirteen-year-old daughter of A. Beketov, a well-known botanist who was rector of St. Petersburg University. We do not know whether the matrimonial-pedagogical idea fell upon barren soil or the girl was simply too young, but Mechnikov was unfortunate in his first choice. Disappointed, he wrote to his mother in the autumn of 1868: "When I fell ill, the Beketovs took me to their home, because I could not have recovered in my flat where I was all alone. While living in their house, I had a good opportunity to learn that the dear children were perfectly indifferent to me, particularly the one to whom I was most attached.... So my fond plans went awry. I was much upset by this, because, next to my scientific work, this undertaking was closest to my heart."

At the end of that same year, however, he married L. Fedorovich, who was Beketov's niece. He made this decision, too, as a result of a certain type of "emotional" reasoning so characteristic of him. This is clear from another letter to his mother written in December 1868 in answer to the one in which she expressed her apprehension about her future daughter-in-law's weak health. "The fact that I knew Lyudmila long before I decided to marry her may show you that there are chances in favour of my judging her soberly and that this is not an infatuation.... Besides, I have a strong affection for her—which is a reliable foundation for future happiness, although I shall not try to assure you that we shall live the rest of our days together as two turtle-doves. I am far from imagining our distant future as enveloped in a kind of rosy haze...."

In spite of all the reservations on the part of the young man, the newly-weds were very devoted to one another. The sad story of this short-lived marriage shows that Mechnikov loved his wife dearly. They might have been very happy indeed but for Lyudmila's poor health.

Owing to her illness—tuberculosis of the lungs—their situation, which was already precarious, grew still worse. The St. Petersburg climate was injurious to Lyudmila's health and the Mechnikovs were obliged to go abroad—to Italy and Switzerland. She improved but was required to remain there. Mechnikov, who had not interrupted his research during all this time and was worn out suffering

from his eye ailment, returned to St. Petersburg but did not stay long. He was again given a commission abroad and accompanied his wife to Villefranche, on the Mediterranean coast, where he was engaged in zoological research resulting in a great measure of success.

In the autumn of 1869, an event of great social significance occurred, involving the fate of another prominent Russian scientist, the physiologist I. Sechenov. Mechnikov was blackballed for the post of professor at the Medico-Chirurgical Academy. This episode was very typical of those benighted years and enfolded itself as follows: Sechenov, who was professor of physiology at the academy, nominated Mechnikov for the chair of zoology, but reactionary-minded professors would have none of him. First, they refused to discuss his candidature on purely formal grounds—Mechnikov's status entitled him to no less a post than that of professor in ordinary, but zoology, a subject of secondary importance in medical education, could hardly be represented by one. When, however, this far-fetched argument was defeated and Sechenov demanded his nomination to be put to a vote, the result was thirteen negative votes out of twenty-five. Sechenov himself described this incident in vivid terms in a letter to Mechnikov dated November 16, 1869: "I am writing to you, my dear and kind Ilya Ilyich, with a very heavy heart. On the one hand, I feel that I am to blame for having involved you in an undertaking which ended in failure; on the other hand, I cannot free myself from the feeling of indignation and disgust provoked in me by yesterday's procedure in voting. This is how it all happened. As you know, I nominated you as a professor in ordinary and the commission which studied your work supported me. When its findings were announced, I declared once more at the Council meeting that you desired the post of professor in ordinary only. The legal and rational thing to do after that would be to vote for or against you, but the President, and with him, Junge and Zabelin, the leaders of the 'young party' of the academy, demanded to vote on the question as to whether the academy needed a professor of zoology at all. This unfair and illegal proposal, together with the rumours that I had recently heard . . . clarified at once their attitude towards you—the worthy gentlemen of the 'young party' did not want you among them and, at the same time, did not want to disgrace themselves by blackballing you.

"As this conviction grew on me, I began to protest in very strong terms against the illegal proposal of the President (since my proposal had met with no opposition). I was guided in what I did by the following consideration: since Messrs. the professors were determined not to have you at the Academy, let them disgrace themselves publicly by blackballing you. Since the President's proposal was completely illegal, your candidature was put to a vote.

"Everybody had dropped his vote into the urn. Junge's turn came. He began to manufacture all kinds of difficulties, saying that two problems had become confused. He was told that since everybody else had decided on voting, he was not entitled to a reargument. He then rose from his seat and treated us to a pompous speech, saying that 'Mr. Mechnikov's merits as a scientist are enough to gain for him the title, not merely of professor, but of academician, but I am convinced that our Academy does not need a professor of zoology and so I vote against him.'

"And such is the irony of fate that it was his black ball that decided your fate, since there were thirteen black and twelve white balls.

"Believe it or not, but this ghastly comedy so shocked and distressed me that I wept. It was a good thing I managed to hide my face. It would have pleased the learned flunkeys around me.

"I beg your pardon once again for letting myself be deceived as regards the moral make-up of most of my worthy colleagues. But, at the same time, just look what a cesspool you might have found yourself in had you been

elected! I was unable to find the words to address that assemblage about your lecturing as an outsider at the Academy and I tell you frankly that I will not try to in future. Henceforth I shall not even enter the Council." (From a collection *Fight for Science in Tsarist Russia*, 1931, pp. 53-55.)

And indeed the incident described above served as the final argument for Sechenov's departure from the place he so detested, and about a year after this, he resigned from the Academy.

Dark thunder-clouds seemed to gather over Mechnikov's head and the prospects before him were gloomy. But in November 1869, he was overjoyed at receiving an invitation to accept the post of professor at Novorossiisk University left vacant by Markuzen, who retired. He was elected to the post in early January of the following year, given a commission abroad to study marine animals and returned to Odessa in the autumn of 1870. For the next eighteen years Mechnikov lived in Odessa, where he was a professor at the university for twelve years. This was an important period in the great biologist's life, one devoted to teaching and major research in zoology.

* * *

This eventful period in Mechnikov's life was replete with joys and sorrows which he took very much to heart.

The first years of his second tenure at Novorossiisk University were highly enjoyable, largely owing to the excellent staff of professors, including such outstanding naturalists as Tsenkovsky, Alexander Kovalevsky, Sechenov and Umov. Mechnikov—vivacious, witty, brilliant and kind-hearted—was the centre of a closely knit group of friends. The members of this group often worked together in the laboratory, discussed scientific problems, and after hours, met almost every day to play music, or read or simply walk. Mechnikov proved to be an excellent teacher—his lectures on the general theoretical problems of

Ilya Mechnikov in 1870

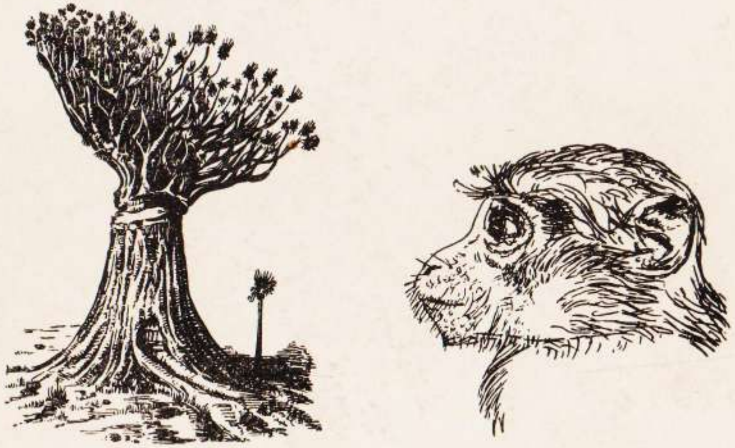
biology abounded in factual material, often the result of his own research, his language was vivid and colourful and his delivery impassioned. All this made him very popular with the students who flocked to his lectures and with bated breath drank in his every word. This is how Y. Bardakh, a favourite pupil of Mechnikov's who later became a professor at Odessa University, describes his professor: "He was all movement—his right hand was held a bit to the right in a characteristic gesture; a torrent of impassioned sentences flowed from him, now and then illustrated with experiments and drawings; pieces of coloured chalk seemed to fly in the air and instantly there was a beautiful and clear drawing on the blackboard showing the evolution of some worm or ascidian. He presented his material in a picturesque way, there were brilliant and quite unexpected comparisons snatched directly from life, astonishingly apt and convincing." [*Vrachebnoye Delo* (*Medical Practice*), 1925, No. 15-17.] Another of his pupils, the well-known bacteriologist V. Khavkin, said that, "in teaching, Ilya Ilyich set himself philosophical aims and succeeded in influencing the minds of his students."

At that time, Mechnikov gave first consideration to the affairs of the university and thanks to his energy and persistence such famous scientists as Sechenov and A. Kovalevsky came to work there. The Ministry of Public Education had long been strongly opposed to Sechenov's appointment in Odessa. Kovalevsky became a professor in Odessa in March 1874, on leaving Kiev University where he had not been appreciated. Mechnikov did not confine his interests to the physics and mathematics department where he was professor, but took an active part in the life of the university as a whole, invariably supporting the student youth and progressive-minded professors.

A striking example of Mechnikov's social and pedagogic interests is his memorandum, "The Need for Activating the Work of Teachers of Descriptive Natural Sciences at Russian Universities," which he wrote shortly after he took up his post at Odessa University in the early autumn of 1870. He began this remarkable document with a statement that the level of scientific research was very high at Russian universities. "Thank God, at present we have so many scientists that we could fill several academies with them." He went on to propose concrete measures which would enable university instructors to combine teaching with research, as, for instance, the proposal to grant the zoologists leave from the end of March to May and from the end of June to September to study marine animals. To prevent these interruptions from affecting the unity and continuity of the course of lectures, he proposed to concentrate the teaching during part of the term and to alternate it with scientific trips. Mechnikov's idea is very akin to the structure of the present teaching schedules in several disciplines where the concentration of lectures in one term enables instructors to devote the other term to research. His idea of combining teaching with research is in complete harmony with our own present-day views on the subject. "The progress of natural science in recent years," he wrote, "demonstrates that it is the university professors (with a very few exceptions) who promote the advancement of science. . . ." "We may accept it as a proven fact that scientific research not only can but must be combined with teaching, and today you will rarely find an academician who does not teach." The following is an expression of pride in Russian science: "The time is not far off when our young scientists will not have to go to German universities. When they go abroad they will go there as full-fledged scientists completely equipped for independent research."

* * *

At the end of 1872 Mechnikov's wife grew much worse. He was summoned to Madeira where she was living and upon his arrival he saw at once that there was no hope for her recovery. Lyudmila Mechnikova died on April 20, 1873. This misfortune so aggravated his eye disease that he was again unable to work with a microscope. But Mechnikov remained true to his vocation as a naturalist and even under those difficult conditions, he wrote an essay on the flora and fauna of Madeira which he graced with his own illustrations.



Mechnikov's drawings from nature done in Madeira

His bereavement was followed by difficulties at the university and disappointment in connection with the Baer Prize. Two persons contested for the Baer Prize in 1873: Mechnikov and Edmund Rusov, a docent of Dorpat University, a botanist specializing in the morphology of lower plant life. Mechnikov handed in three scientific works, one printed and two in manuscript, one of which was the classic *Investigation of the Evolution of Medusae and Siphonophora* destined to win world fame. The prize was adjudicated by a special commission appointed by the Academy of Sciences, whose decision was final and was announced to the assembly of academicians of the Biological Section of the Physics and Mathematics Department. On February 17, 1873, Academician Karl Maximovich, a botanist, announced the following decision of the commission: "Having thoroughly discussed the contestants' works and listened to the critiques made by scientists specializing in the subjects whom the commission invited for the purpose, in conformity with previous practice, the commission pronounced both of the contestants worthy of the prize." (*Proceedings of the Academy of Sciences*, Vol. 22, 1873.) In crying contradiction to this preamble, the commission awarded the prize to Rusov while the name of the second claimant was never as much as mentioned. As time went on, the details of this unsavoury procedure came to light. It transpired that the commission was split in two groups, one of which (including Academician Maximovich) supported Rusov, despite his being a botanist and despite the fact that the conditions of the contest favoured works on embryology since Baer was an embryologist *par excellence.* Other members of the commission, including Academician F. Ovsyannikov, an outstanding physiologist and histologist, and Academician N. Zheleznov, a botanist, supported Mechnikov. A discussion ensued and the majority expressed themselves in favour of examining the papers once more. Rusov's work was sent for review to a well-known German botanist, A. Braun, Rusov's teacher, who naturally reported favourably on it. Another, rather ridiculous, argument on behalf of Rusov was that his work had been printed while two of Mechnikov's works were in manuscript form. This was considered to be a weighty argument in favour of placing Mechnikov second, although the conditions of the contest did not preclude the award of the prize for an untyped work, but only provided for some delay. Although armed with all these arguments, Mechnikov's opponents on the commission (who constituted the majority) did not dare to refuse his claim but suggested dividing the prize between the two. Mechnikov's supporters vigorously protested against this and the prize went to Rusov.

The decision of the commission aroused public indignation. Eminent scientists, such as A. Beketov, N. Zheleznov and A. Kovalevsky gave vent to their anger at the sessions of the Society of Naturalists and in the press. In the autumn of that year, Mechnikov wrote in *Golos* (*Voice*) with sarcasm: "I cannot believe that a learned commission would regard the fact that a work has been printed as its intrinsic virtue. If we start from this premise, we may come to appreciate a work on the merit of the number of its pages, the beauty of the penmanship, the quality of the paper, etc."

The discussion lasted till 1882, nearly ten years, and the incident conferring little credit on the Russian Academy of Sciences came to an end in 1891 when Mechnikov, who had long given up his study of embryology, received the prize awarded him as a result of the initiative on the part of several famous biologists "for all of his work on embryology done in the course of the past decade."

All his troubles drove him to attempting suicide by taking morphine. The dose he took, however, caused only vomiting and this saved him. He was enveloped by melancholy for months afterwards and still entertained the idea of suicide. Yet his interest in science overcame his despondency and Mechnikov returned to his work.

This is how he himself described this turning-point in his life. It was in Geneva, on his way back from Madeira. One evening he was walking on the Rhone embankment, preoccupied with thoughts and plans of suicide. He saw clouds of insects swirling round the flame of a gas lantern and he mistook them for ephemeras which live only a few hours as grown insects and have an underdeveloped digestive tract. Mechnikov asked himself how the theory of the survival of the fittest could be applied to them since they did not eat, took no part in the struggle for existence and, consequently, could not adapt themselves to their environment. The posing of this question, to which there seemed to be no answer, supplied the impulse which served to return him to normality.

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The summer of 1874 found Mechnikov in Odessa where he resumed his duties at the university. In 1875, he married Olga Belokopytova, a seventeen-year-old girl who had an agile mind and was interested in natural sciences. Mechnikov had taught her zoology; a friendship then developed between them and when Olga became his wife, she mastered histology and microbiological technique, helping him in his work. She had a talent for painting and clay modelling—her works were often displayed at art shows. She did several very good portraits of her husband.

At last, Mechnikov's dream had come true. He had a wife who was his pupil, friend and assistant, and he was very happy with his young wife.

We have mentioned elsewhere that the Odessa period, filled with various interests, was a fruitful one in Mechnikov's life, but it did not last long. Ominous clouds began to gather on the political horizon; in Odessa University, as in other parts of Russia, reactionary forces launched an offensive, and in the middle of 1882, Mechnikov left the university. He spent the summer at Popovka, his wife's estate in Kiev Gubernia, and in the autumn went to Messina where we met him at the beginning of our story.

MECHNIKOV AND EVOLUTIONARY EMBRYOLOGY

The years, during which Mechnikov began his scientific career, witnessed the most important turning-point in the history of biology—the appearance of Darwin's *Origin of Species* and the triumph of the new evolutionary theory. The vast factual material accumulated in the various branches of biology—morphology, classification, comparative anatomy and zoogeography—had to be explained in the light of that theory. On the other hand, the young and yet immature Darwinism, already vigorously attacked by its opponents, was in need of support from various aspects of biology, requiring new facts and new generalizations to strengthen its main premises.

Darwin's theory, one cornerstone of which was the thesis of a relationship existing among all organisms, was the first to establish that embryology was one of the means of clarifying these relationships. Proofs supplied by embryology (along with those of comparative anatomy and palaeontology) are among the chief weapons in the arsenal of Darwin's theory of evolution. Most of the credit for this is due to F. Müller who was the first to confirm Darwin's principles by demonstrating the evolution of certain invertebrates (Crustacea) in his *For Darwin* written in 1864.

The status of embryology, however, was rather weak. One of the oldest sciences, dating back to Aristotle, embryology by the mid-nineteenth century had amassed extensive material on the evolution of different animals, but this material was haphazard and incomplete. Data on the embryology of the vertebrates were relatively abundant. By the second half of the eighteenth century, the development of the chick embryo had been described in considerable detail by K. Wolf, an academician from St. Petersburg. In 1817 another St. Petersburg academician, K. Pander, discovered for the first time the presence of three germ layers in the chick embryo, which he called serous, vascular and mucous. The famous K. Baer had made an important contribution to embryology: it was he who discovered an ovum in the graafian follicle of the dog, thus providing a correct description of the mammalian ovum. He also formulated, in precise terms, the theory of germ layers, a theory so important for embryology. In addition, he gave a detailed description of the germ layers, a most important evolutionary acquisition of the higher vertebrates (reptiles, birds and mammals). It can be said that Baer put vertebrate embryology firmly on its feet, leaving to scientists who came after him the task of clarifying the details of development and evolving the general laws governing it.

The picture was entirely different in the case of invertebrate embryology. Research workers had vast unexplored areas to study.

* * *

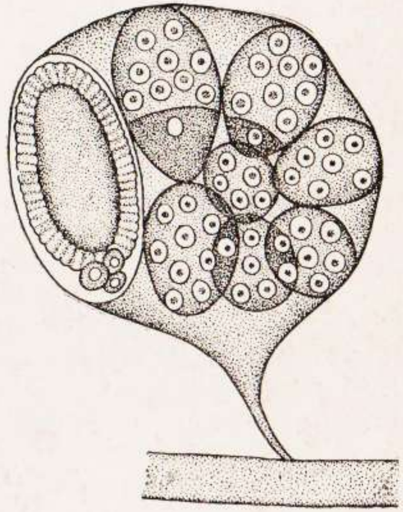
The works of Alexander Kovalevsky and Ilya Mechnikov enriched science with much factual material and theoretical conclusions of exceptional significance. It would not be an overstatement to say that they founded a new branch of biology—comparative embryology—which yielded data in support of Darwin's theory of evolution.

During the twenty-one years of his work in embryology (1861-82), Mechnikov completed 43 theses, not all of equal value. The following four are of paramount significance: *The Study of Insect Embryology* (1866), *Research in the Development of the Echinodermata and Nemertinea* (1869), *Materials for the Study of the Siphonophora and Medusae* (1872) and *The Embryological Study of the Medusae* (1886). Although the last-cited work was published after what we are pleased to call the "embryology period," its content places it among the works of that period, all the more so since it was actually written at the end of the seventies and beginning of the eighties. It is not necessary to list here all the works belonging to that period. It will suffice us to follow the progress of Mechnikov's interest in embryology and to mention the most important results of his unceasing efforts during those two decades.

* * *

Mechnikov did not suddenly take up research in the sphere of comparative embryology. His first work on embryology was accidental, prompted as much by his interests in new and vital problems as by his love of argument. In the early sixties, biologists were excited by the discovery of an original type of reproduction in the Cecidomyia—gall-flies (or gnats) made by Professor N. Wagner of Kazan University. These two-winged flies live on the leaves of certain plants, producing galls on the leaves. Wagner discovered that within the larvae of these insects there appears a new generation of larvae which devour the entrails of the parent larvae and then become free-living. The similarity of the two generations of larvae, the complexity of their structure and the universal occurrence of this phenomenon precluded the idea of the larva body being invaded by parasites. Wagner assumed that this represented the alternation of sexual and asexual generations, the daughter cells coming not from eggs but from the cells of the adipose tissue of the parent larva. Wagner's *Spontaneous Reproduction of Caterpillars in Insects* was published in 1862, but the world of science received it coolly, and the weighty opinion of K. Baer, who confirmed the correctness of Wagner's observations and nominated him for the Demidov Prize of the Academy of Sciences, was required for the scientific world to accept the discovery. Scientists were stimulated

to study the details of this new and interesting question. At the time Mechnikov was in Giessen (1864), Leuckart's laboratory was engaged in studying this problem. Leuckart shared Wagner's opinion and further stated that the daughter larvae are produced by structures not unlike those occurring in the usual embryonic chambers of other insects. But since those were not true egg cells, Leuckart proposed to call them by the recently introduced term "pseudovum." In his work, Leuckart mentioned Mechnikov's name but did not specify what the latter had done. In an article which he published in 1865 in a widely circulated German journal *(Arch. f. Anat., Physiol. u. wiss. Med.)*, Mechnikov stated that he was the first to have observed in his laboratory the formation of the embryonic larvae. He went on to state that, in a controversy with Leuckart, he had expressed the opinion that the second generation emerged from true egg cells, i.e., that it was an instance of parthenogenesis. Another article, entitled "On the Development of the Cecidomyia Larvae from Pseudovum," published in that year in the *Arch. f. Naturgeschichte*, also dealt with this problem. In it Mechnikov presented weighty proof that reproduction in the gall gnats was truly sexual. He had established that this was an instance of what is known as superficial cleavage in



Ovary of Cecidomyia containing pseudova at different stages of development (from a drawing by Mechnikov) insects and that the cells from which the larvae developed were true eggs containing a nucleus (germinal vesicle). At first, Mechnikov's idea was rejected. M. Ganin, a Russian zoologist who had been at Kharkov University at approximately the same time as Mechnikov and who specialized in insect embryology studying paedogenesis in gall-flies, expressed his disagreement with Mechnikov. His opinion was that in the case under discussion the egg was formed by the fusion of several cells and was not a typical germ cell. To settle the controversy, Mechnikov turned to Baer, forwarding from Munich, on June 23, 1866, his article entitled "An Investigation of the Diptera. A Letter to K. M. Baer," criticizing Ganin's view. Baer sent it to the *Transactions of the Academy of Sciences* (Vol. X, 1866) and wrote to Mechnikov that, although he differed from him on some details of terminology, he concurred in his basic views. That Baer had a high opinion of Mechnikov even at that early date can be seen from the following: "I rejoice in your energy and abilities and trust you will be a credit to your country." At the same time, he suggested that Mechnikov should refrain from controversies and cited Cuvier and Humboldt as examples (Baer's letter written in 1868). A reserved old man, Baer could not understand Mechnikov's ardour, although he appreciated the younger man as a scientist. In his letter, Baer advised Mechnikov to submit his work on the Diptera and to contest for the first Baer Prize. This Mechnikov eventually did.

Time proved that Mechnikov's view in this dispute was correct and today it has been established with finality that paedogenesis in Cecidomyia is an instance of true parthenogenesis.

* * *

The study of the development of gall gnats was the first in a series of investigations conducted on the development of insects and the Arthropoda generally. During

his short stay abroad, Mechnikov studied the development of insects (including the Hemiptera, the Aphididae and the Diptera), the Arachnida (scorpions), and round- and flatworms.

His choice of insects as the main object of study was not accidental. As has been mentioned above, during this period, the ideas of evolution had scarcely penetrated the sphere of embryology. The accepted notion was that the evolution of different classes (to say nothing of types) of animals proceeded in different ways, that there were no principles common to groups far removed from one another. It was considered that even the important evolutionary stages in different classes had nothing in common. This viewpoint was akin to the old pre-Darwinian idea of embryology, holding that there were different "types of development," an idea born of the vague, idealistic German *Naturphilosophie* which denied the existence of any genetic relationships among different groups of animals. The young German scientist Weismann, who later became widely known for his idealistic views on heredity, was at that time a somewhat modernized advocate of that antiquated idea. At the Congress of Naturalists and Physicians in Giessen (the first scientific assembly which Mechnikov attended), Weismann read a paper on the development of gnats and flies.

In later years, Mechnikov was of the opinion that Weismann's work had impressed favourably those present because of its seeming thoroughness and the detailed method of presentation. The main conclusion of Weismann's work was that development in insects proceeded in a perfectly original way and that no parallel could be drawn between the arthropods and the vertebrates. As Mechnikov said, "Weismann particularly stressed" the absence in insects of germ layers, homologous to those in higher animals. In Weismann's opinion, that which some authors took for germ layers were actually folds found only in insects and in no other group of animals.

Alexander Kovalevsky
(1840-1901)

Such assertions were at marked variance with the theory of evolution of which Mechnikov was a champion. We may rightfully assume that his disagreement with Weismann's theoretical premises and his desire to study the development of arthropods himself prompted him to choose precisely those very animals as the object of his early research in embryology. He was able to prove Weismann wrong; he discovered germ layers similar to those in higher vertebrates in all the representatives of the arthropods he investigated. A by-product of his research were the observations on the peculiarities in the development of insect eggs as determined by an excess of yolk. He studied in detail superficial cleavage observable only in the development of these animals and explained the role of the folds, or membranes, (which Weismann failed to see). He called these amnion and chorion, corresponding to the terms designating similar structures in higher vertebrates. These observations were the first steps Mechnikov took along the road towards establishing the existence of common stages in the development of taxonomically distant animal groups and were also the first steps in the development of a new science—comparative, or rather, evolutionary embryology.

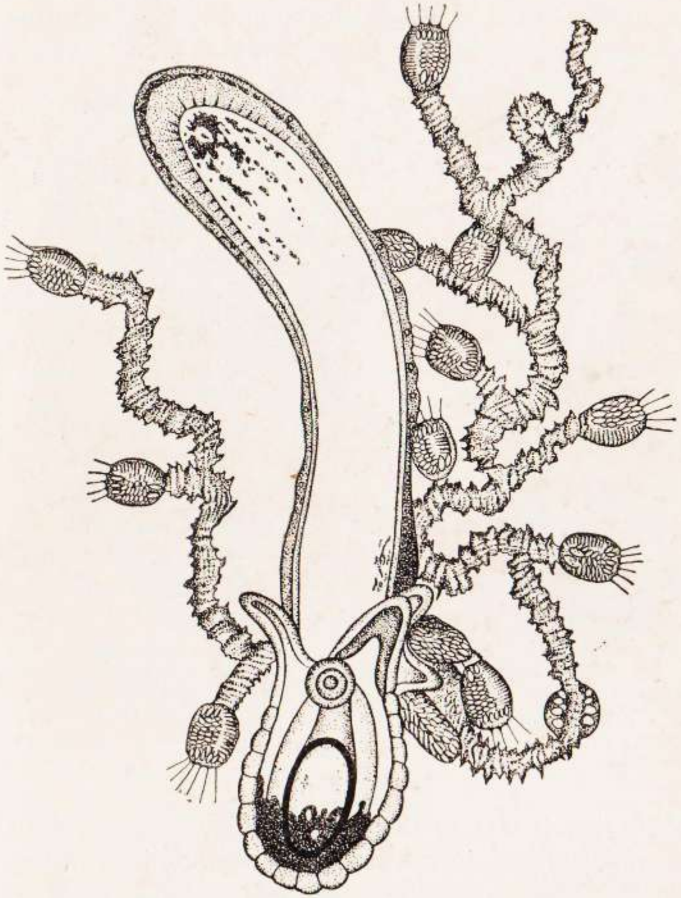
Beginning with the second half of the sixties, Mechnikov's investigations proceeded along lines parallel to those of Alexander Kovalevsky, an outstanding Russian scientist and very congenial person with whom Mechnikov had established close personal contact. Mechnikov wrote later that in 1864 Kovalevsky started a systematic study of the development of certain living organisms with a view toward proving the fundamental principles of Darwin's theory as applied to embryology. The two scientists met for the first time in the summer of 1865 when Mechnikov came to Naples to study marine fauna, but they had corresponded for some time previously. It was Kovalevsky who encouraged Mechnikov's interest in marine animal embryology, and since 1865 the latter devoted all his energies to the study of various lower invertebrates. He interrupted this study for short intervals when he conducted purely morphologic investigations (for instance, to describe a new class of the Gastrotricha or a new group of lower multicellular organisms, the Orthonectida).

Between 1865 and 1869, Mechnikov worked very hard and completed about thirty treatises on the development of different classes of lower animals, such as the Suctoria, tapeworms, Nemertinea, Rotifera, ringworms, Turbellaria, Gastrotricha, Mollusca, insects and the lowest of the Chordata, the Balanoglossus belonging to the Enteropneusta.

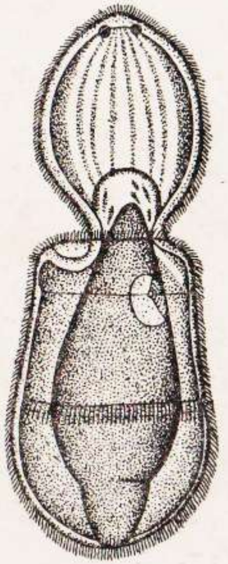
The following five years (1869-74), during which Mechnikov continued studying these forms, and, in addition, the Crustacea, were also very fruitful. These investigations, conducted simultaneously with Kovalevsky, enabled the researchers to establish beyond doubt that all the animals investigated, regardless of their place in systemic classification, possessed the two basic germ layers—ectoderm and entoderm—and developed in accordance with general laws. This provided new *embryologic* proof of the unity of the entire animal kingdom. The conclusion to be drawn from their work can be expressed as follows: germ layers are homologous in all multicellular animals, since they are similar with respect to their position and role in the processes of organogenesis.

As we have pointed out before, Mechnikov became a convinced adherent of the theory of evolution at an early age. It was for that reason that he began the investigation of individual groups of animals whose relationship to one another was not clear at the time, such as the Siphonophora, the Kinorhyncha, the Gastrotricha and the Enteropneusta. The existence of these groups with undefined origin seemed to contradict the monophyletic principle on which the evolutionary theory was based and which Mechnikov whole-heartedly supported. His research was complex, combining the descriptive-morphological method with the indispensable study of development and, in later years, with physiological research in zoology.

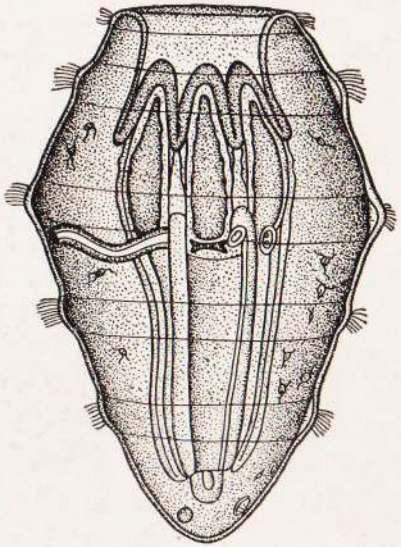
In many cases, his investigations were successful, enabling him to establish the relationship existing among the seemingly unrelated groups of animals and to assign to them their correct place in the system of classification. Thus, Mechnikov's discoveries established the relationship between the Siphonophora and the Hydrozoa; his discovery of metagenesis in scyphozoan medusae helped to establish the relationship between jellyfish and other groups of the Coelenterata. He was able to throw light on a very important biological phenomenon known as metagenesis or alternation of generations. Mechnikov's greatest achievement was the clarification of the taxonomy and relationships of the Enteropneusta which were little known in his time. The Balanoglossus belonging to this group had been regarded as a worm because of its elongated body and the presence of a proboscis. Mechnikov proved, first, that the larva of Balanoglossus is the tornaria, which previously had been taken for an echinoderm larva, and secondly, that the development of the tornaria is somewhat similar to that of a typical



Larva of siphonophore, a free-swimming coelenterate (from a drawing by Mechnikov) echinoderm, particularly of the starfish. The brilliant research of Kovalevsky accomplished at approximately the same time showed that the development of the tornaria was similar to that of the Protochordata, such as ascidian and lancelet. It was in this way that the genetic relationship among three forms, all quite different in external appearance—the Echinodermata, the Enteropneusta and the Chordata—was proved. In all the three groups, the blastopore either disappears in the course of embryonic development or becomes the anus, unlike other multicellular animals where the blastopore becomes the mouth of the adult form. This fact prompted Mechnikov to divide all multicellular animals into two groups: the protostomia or those in which the blastopore is the mouth and the deuterostomia or those in which the mouth of the adult form develops anew. This division has proven valid to this day.



Larva of the Balanoglossus belonging to the Enteropneusta (from a drawing by Mechnikov)



Auricularia, in echinoderm larva (from a drawing by Mechnikov)

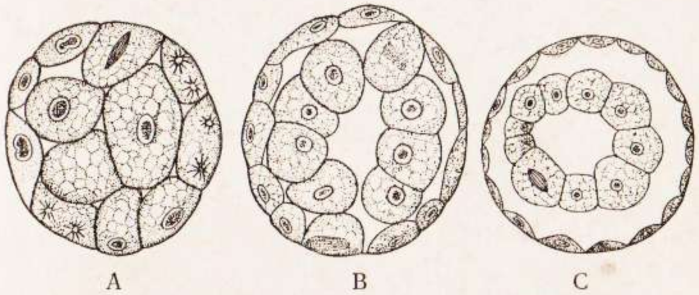
Mechnikov also discovered a certain similarity even in the adult forms of the Echinodermata and Balanoglossus. He considered the firm and resilient proboscis in the latter homologous to the ambulacra of echinoderms which serve most of them as organs of locomotion.

The similarity among different groups of the deuterostomia proved to be still more striking when Mechnikov investigated one of the most important stages of embryonic development—the formation of the coelom. He found that in the Echinodermata, the tornaria and the Protochordata the coelom arises as the enterocoele. At the blind end of the original enteron or gut, there appears a double outgrowth which divides by transverse fission, producing three pairs of coelomic vesicles on either side of the enteron, the anterior pair coming into contact with the outside world at a certain stage of embryonic development. This trimetameric formation of the coelom (with certain variations) proved to be characteristic of the embryonic development of all deuterostomia. Mechnikov, however, went even further: in studying the development of lower multicellular animals such as medusae and ctenophores, he discovered a similarity between the position of the most important organ of the latter—the gastro-vascular system—and of the coelom in the larvae of the Echinodermata. His own careful observations and a study of scientific data provided him with grounds to suppose that the coelom of the Coelomata is homologous to the peripheral part of the gastro-vascular system in the Coelenterata. But since the development of the Echinodermata possesses features in common with the Enteropneusta and Chordata, an uninterrupted series of coelom formation can be observed, beginning with the Coelenterata, through the Echinodermata and the Enteropneusta to the Chordata. The classic research of Mechnikov and Kovalevsky proved to be of great significance for phylogenetics, the science treating of the genetic relationships among animals, since these relationships were clarified and, in some instances, established anew.

His study of the embryonic development in the Echinodermata provided Mechnikov with other data of value to embryology. In his brilliant work, *Research in the Development of the Echinodermata and Nemertinea* (1869), he proved that the adult forms with radial pentamerous symmetry are preceded by an embryonic stage in which the water-vascular system is bilaterally symmetrical, describing how a bilaterally symmetrical larva becomes an adult form with the characteristic pentamerous system. He observed the formation of the water-vascular system from the coelom of the larva and drew far-reaching conclusions in the sphere of comparative anatomy, viz., that the section of the water-vascular system communicating with the environment, the madreporic canal, might be compared with the gastro-vascular canals of the upper section of the body in the Ctenophora.

Mechnikov is the author of many other works in the field of embryology and morphology. He described hitherto unknown methods of differentiation in two-layer embryos, multipolar migration and delamination; he discovered a rudiment of the mesoderm in Callianira, a representative of the Ctenophora, etc. Throughout the first period of Mechnikov's scientific career, Kovalevsky encouraged his interest in embryology, a branch of biology which, at that time, had special significance. Mechnikov, too, influenced his friend's interests: Kovalevsky's brilliant works on the comparative physiology of the excretory organs in the invertebrates (1888), for instance, are related in spirit to Mechnikov's works on phagocytosis and were conceived apparently as a result of direct suggestion.

Although Mechnikov and Kovalevsky were personal friends and possessed common scientific interests, it would have been difficult to find two men more unlike in mental make-up, character, and methods of research. Mechnikov was a theoretician attracted to general scientific problems, given to making broad philosophical generalizations, impetuous and quick in his conclusions, sometimes apt to disregard facts but self-confident and persistent in the attainment of his aims. Kovalevsky, on the other hand, was an empiricist, tackling only concrete tasks, avoiding (we may even say, fearing) "all that lofty theoretic stuff," but at the same time extremely precise and thorough in his observations. A modest, mild and yielding man in everyday life, he was firm and indomitable in scientific disputes concerning facts which he knew well and had verified many times.



Formation of gastrula by delamination in a medusa. *A*, *B* and *C* are the stages of the process, the upper part of the left-hand figure showing the transverse cleavage of a cell as a result of which the inner germ layer, or hypoblast, is formed (from a drawing by Mechnikov)

It is no wonder, then, that the two scientists working side by side on a problem, often on the same subject, disagreed (sometimes very materially) on certain aspects of the problem and, having arrived at different conclusions, vigorously defended their respective viewpoints. Thus, Mechnikov denied that the formation of the digestive tract in lancelet took place by a process of invagination; he held that the nervous system in the ascidium larva was formed from the entoderm, while Kovalevsky correctly asserted that it was formed from the ectoderm, and so on. Mechnikov, volatile and impatient, was usually the one who started a dispute, and, not content with speaking his mind or writing to his opponent, he would denounce Kovalevsky's views in print—in the *Naturalist* journal. Deeply hurt, Kovalevsky would repeat his experiments over and over again and when they corroborated his original conclusions, he would mildly but firmly reassert his opinion. We must add, in justice to Mechnikov, that when time and the work of other researchers proved Kovalevsky right, Mechnikov himself would be convinced and would openly admit his mistake (as was the case with the nervous system in ascidium). In this way, truth was born out of dispute and the two remained fast friends till Kovalevsky's death in 1901.

* * *

It was for his work on embryology that Mechnikov was awarded his scientific degrees. He received his master's degree in 1867 for his paper on the development of sepiola, in which he proved that germ layers can be observed even in this cephalopod mollusc. A year later, he presented his doctor's thesis, entitled "The History of the Development of Nebalia," dealing with a genus of the Crustacea belonging to the order of the Leptostraca. Curiously enough, the two theses were not among the best of Mechnikov's works. Certain factual errors were clear even then, to say nothing of later times with their advances in the science of embryology. One of the errors Mechnikov made was that he observed only two germ layers instead of three in the Crustacea. The form of the dissertations, too, was inferior to that of many of his works written before and after. This was probably due to lack of time and haste.

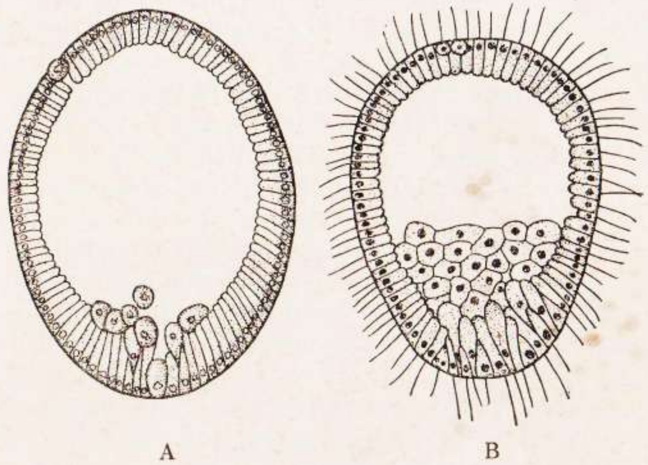
And yet, the contents and even the form of the two dissertations set them apart from the general run; the short interval between his master's and doctor's theses, as well as the scientist's age—he was twenty-three years old—bear eloquent witness to his extraordinary talent. Mechnikov changed his field of study in 1874. From that time on, he concentrated on the study of two types of lower invertebrates, the Coelenterata and the sponges, publishing in the course of the following twelve years four articles on sponges and nine on coelenterates. Among them are: *The Investigation of the Evolution of Medusae and Siphonophora* (about 100 pages), and *The Embryological Study of the Medusae* (160 pages), describing the remarkable phenomenon of metagenesis he had discovered. Other groups of animals were almost entirely beyond his sphere of interest, but he did publish a work on Turbellaria and two on the development of Myriapoda. The latter topic, although little known and but rather important in the study of embryology, may be said to have been chosen by chance. In 1873-74, Mechnikov's eyes caused him a great deal of pain, and, being unable to work with the microscope, he went on an anthropologic expedition to Astrakhan steppes; there, in the Manych area, he came across certain myriapods, whose development was little known, and, equipped with a microscope which he had obtained in Astrakhan with much difficulty, he was able to study the relatively big ova and embryos without overstraining his eyes.

The change in the object of his study and interest in the lowest metazoans was occasioned by the rise of new theoretical problems haunting Mechnikov and carrying him away from Kovalevsky's pursuits. Mechnikov was no longer interested in the universal nature and homology of the germ layers in all animals; he turned his attention to new problems which arose logically from this main premise, i.e., what was the most primitive path of development of a multicellular organism from an ovum, what was the most ancient form in the differentiation of germ layers, and, particularly, whether the knowledge of the earliest stages of individual development of animals could explain the way and manner in which multicellular animals appeared. Evidently, the answers to all these questions could be provided most readily by a study of the simplest of the multicellular organisms.

* * *

Perhaps the reason for his attention to a new field of research must be looked for (as was the case with paedogenesis in gall-flies and the germ layers in insects) in Mechnikov's passion for argument. In 1872, Ernst Haeckel first published his gastraea theory, a theory of the development of metazoans which he further elaborated in 1874. According to this theory, multicellular animals descended from a colony-forming spherical unicellular ancestor resembling the modern flagellate, such as Volvox, which represented a lower phylogenetic stage (blastaea) not unlike a blastula, the spherical stage in individual embryonic development. The two-layer organism, gastraea, was formed through a process of invagination. The inner layer gave rise to the digestive system and the blastopore became the mouth of the new organism. In Haeckel's opinion, gastraea was the common ancestor of all multicellular animals, and the existence of these stages in phylogenesis was reflected in the blastula and gastrula stages in the embryonic development of most higher animals. The gastraea theory was based on Kovalevsky's research proving the presence of the gastrula stage, formed by invagination, in many animals. The theory was presented brilliantly but somewhat schematically.

Haeckel's theory at once aroused vehement opposition on the part of Mechnikov who considered it highly improbable. True evolutionist that he was, Mechnikov firmly adhered to the historical principle in all his theoretical hypotheses. If this principle is to be followed, one should ascertain those stages in the development of the lower metazoans which are closest to the phylogenetic transition forms between unicellular and multicellular organisms, in other words, the stages most closely resembling the blastula and gastrula must be particularly clear here. In this new sphere of embryology, Mechnikov concentrated on the study of the development of sponges and coelenterates and concluded that his doubts were justified. He observed that, in hydromedusae and lower sponges, the simplest organisms in these groups, the ectoderm is formed not by invagination but in a number of entirely different ways. These ways differ in different hydromedusae, but after studying a large number of forms, Mechnikov was able to compile a series of the ways in which the second layer was differentiated, classifying them from the simplest to the more complex, with transition forms between them. He considered the simplest of these forms to be multi-



Formation of gastrula by migration in a medusa. *A* is the first stage showing the cells of the lower (vegetative) pole migrating into the interior cavity, or the archenteron; *B* is a later stage with the migrated cells forming the entoderm, and the ectoderm cells carrying cilia (from a drawing by Mechnikov) polar migration in which groups of cells from different parts of the spherical blastula are deposited in the internal cavity. A variant of this process was unipolar migration in which cells came from one part of the one-layer embryo. The next step in complexity—invagination—was encountered only in more complex animals belonging to the same groups. Here the localized but haphazard migration of cells became a clearly defined process. If this were true, then Haeckel's gastraea theory was proven to be untenable.

Mechnikov considered invagination to be a relatively late adaptive stage in the formation of the second layer, whereas he looked upon migration of the surface cells into the cavity, where they performed the function of digestion, as the simplest, the initial stage. Consequently, he considered that evolution from the simplest multicellular organisms to the more complex had proceeded in a manner entirely different from that which Haeckel described: not from a two-layer sphere—gastraea—but from a one-layer organism, part of whose cells migrated towards the internal cavity. What, then, was the organism like and how had its evolution progressed? This question stared Mechnikov in the face and made him abandon pure embryology for biology in the widest sense of the term. This was one more step along the apparently contradictory road which brought him to that memorable day in December, in Messina.

AUTHOR OF THE THEORY OF METAZOA

What could this original organism have been like?—an organism simpler than the simplest of sponges, in existence during the remotest ages of life on earth, and through which the transition from unicellular to multicellular animals was effected? Like Haeckel, Mechnikov thought that that initial form must have been a spherical colony of flagellates, perhaps one resembling Volvox,

well-known to every schoolboy, or even a simpler one—Pandorina. Pandorina possesses the properties of protozoans and resembles the classic unicellular forms like the *Euglena viridis*, but at the same time, it is a colony, an accumulation of several cells encased in a gelatinous covering. Each of the sixteen perfectly uniform cells of Pandorina has its own flagella and other organoids and can live independent of the rest of the cells. In Volvox, which is related to Pandorina through a number of transition forms, the rudiments of a new and very important property can be observed; this property is a "division of labour" between its individual cells; it is in this direction that further evolution proceeds. A Volvox colony has at least three types of cells: surface flagellate cells which protect the colony from adverse influences and serve as a means of locomotion, inner cells devoid of flagella, which digest food passed on to them by the surface cells, and sex cells, whose function is reproduction and propagation of the species. So this colony of unicellular protozoans possesses the main characteristic of multicellular organisms—groups of specialized cells. Volvox is a modern form but there was a remote ancestor—the connecting link between protozoans and metazoans. What was the impetus to this evolution and in what way did it take place? Mechnikov formulated the following theory as an answer to this question. At some remote time, a colony existed which had all of its cells distributed on the surface, forming a sphere not unlike the blastula stage in the development of multicellular organisms. It was in a state of constant motion which hampered the process of digestion. This can be proved by observing the antagonisms between the different functions in a cell. The struggle for existence necessitated the appearance of a new adaptation: some cells of the organism wandered temporarily inside the organism where, protected by the surface cells, they could conveniently digest food, after which they again came to the surface. The products of digestion spread to the other cells of the colony which began to feed by means of the specialized digestive cells. This new and useful adaptation stabilized, giving rise to a new type of colony possessing a solid inner layer of digestive cells, the parenchyma, and Mechnikov called this hypothetical organism *parenchymella*. In what way did it get its food? Here Mechnikov for the first time noticed a property of cells to which he was to attach major importance in his future work. This property is the ability to engulf and digest solid food particles—an extremely important biological process which he later called phagocytosis, from the Greek *phagos*—to eat and *kytos*—cell. In his opinion, it was this ability which prompted the individual cells of the colony which had enveloped a fragment of food to move to the interior and, in the course of time, to become digestive cells. This was how the first step towards a very important stage in evolution—the appearance of a multicellular organism—was made. Mechnikov considered phagocytosis of such paramount importance that he gave the name of phagocytella to the hypothetical intermediate form, and indeed, it superseded parenchymella. He held that this form gave rise to the simplest of metazoans, sponges and coelenterates.

The virtue of the parenchymella theory lay in the fact that was based on the doctrine of evolution and took into account the method of differentiation of the two layers observed in lower metazoans. According to biogenetic law, it was historically this two-layer differentiation process that in the course of subsequent alterations (often adaptive) gave rise to other means of differentiation—including invagination, Haeckel's favourite. Another advantage of Mechnikov's theory was its physiological approach to the explanation of evolution. The motive power was to be observed in the improvement in the mechanism of obtaining food and its subsequent assimilation, ensuring satisfaction of the organism's need for nutriment. Nutrition, in turn,

is essential for metabolism, an important function and prime condition of life. The improvement of intracellular digestion, according to Mechnikov, provided the stimulus which resulted in the formation of multicellular organisms. These two features of his theory, to say nothing of its minor aspects, should have sufficed for its acceptance as a well-founded and very progressive hypothesis. Yet it was not immediately accorded the place it deserved in the arsenal of fundamental biological doctrines. Haeckel's gastraea theory with its appealing mechanistic simplicity was destined to dominate science for a long time.

The honour for reviving Mechnikov's theory and recognizing its worth goes to Soviet biologists. Chief among them was Academician Alexei Zavarzin who, in his *Essays on Evolutionary Histology of Blood and Conjunctive Tissue*, clearly showed the vast significance of Mechnikov's theory for biology in general. A. Zakhvatkin, a talented embryologist who died at his prime, expounded this theory in detail in his *Comparative Embryology of Lower Invertebrates*. Today many progressive biologists abroad have adopted Mechnikov's theory.

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We have mentioned only such of Mechnikov's works and theoretical ideas which determined the main sphere of his scientific research during the first twenty years of his work in zoology. During this period, he completed a number of other fairly significant works, but the ones we have described should suffice to indicate the important contributions he made to the various general branches of biology.

However, perhaps it is most significant that Mechnikov and Kovalevsky ushered in the classic period in Russian morphology. Their co-workers, pupils and followers —V. Zalensky, M. Ganin, N. Bobretsky, A. Korotnev, A. Ostroumov, V. Shimkevich and many others—did so much for the development of zoology that the latter half of the nineteenth century is, not without justification, called the "Russian period" in the history of this science.

Had Mechnikov confined himself to the sphere of evolutionary embryology alone, developing the theory of the appearance of metazoans and nothing more, this, in itself, would have served to immortalize his name. Actually, it was but a stage in his career, a step on the road of constant search, which he pursued his whole life.

DOCTRINE OF INTRACELLULAR DIGESTION. BIOLOGICAL FUNCTION OF PHAGOCYTOSIS

His study of the difficult problem of genetic relationships in the animal kingdom and, in particular, of the origin of the Metazoa, proved to Mechnikov—probably in the latter half of the seventies—that the morphological method alone was insufficient. He confesses this quite plainly in his *Investigation of Intracellular Digestion in Invertebrates* (1883), marking a new stage in his research—a logical continuation of the preceding one: "While studying some problems of metazoan genealogy, I became convinced that such problems cannot be solved by the methods provided by morphology and embryology alone. Although morphology [i.e, general morphology or embryology.—*S.Z.*] attaches prime importance to atrophied organs which have ceased to function or to organs in the process of formation most of which have not yet begun to function, in order to establish the genealogic significance of such organs one is often obliged to know their *physiological history*."* (*Selected Biological Works*, 1950, p. 246.) This prompted Mechnikov to turn from comparative embryology to comparative physiology.

As the subject of his investigations, he chose digestion inseparably connected with metabolism. As far back as his

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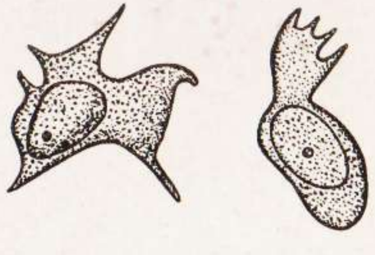
* My italics.—*S.Z.*

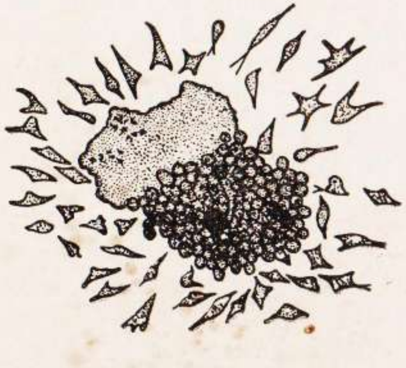
Giessen period, while studying *Geodesmus*, a planarian, he discovered intracellular digestion in it; food which entered its body by way of the oral opening was enveloped by special cells and digested within their protoplasm.

His studies in embryology and zoology over a long period of time showed Mechnikov that intracellular digestion was a widespread phenomenon and could be observed not only in protozoans but also in simpler metazoans, such as sponges, coelenterates and in some flatworms (the Acoela). Even when these groups possess a digestive cavity, it serves only for storing food until final digestion. The cells forming the cavity are highly phagocytic, they are able to envelop and ingest food particles, to digest them with the aid of special enzymes contained within their protoplasm. The products of digestion are then carried to all parts of the body (regardless of size) along intercellular ducts and canals of the gastral system. Intracellular digestion was thus found to be more common than was generally supposed and to occur not only in protozoans. Mechnikov then asked himself—might this biological phenomenon be encountered on higher rungs of the zoological ladder, where this method of digesting ordinary food had been superseded by a more complicated method? Perhaps this phenomenon might be observed even in those organisms having intracoelomic digestion?



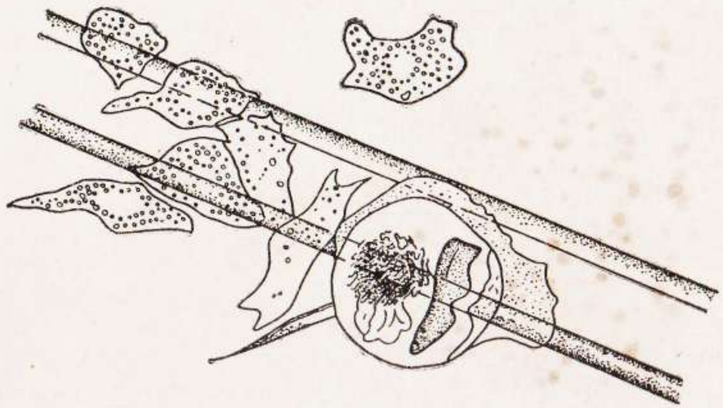
Amoeboid cells in the body of a medusa (from a drawing by Mechnikov)

His numerous observations confirmed this idea; Mechnikov concluded that phagocytosis was a biological function common to a great variety of animals, found in different cells and not confined to the digesting of food as such. Among phagocytes, the most prominent are meso-



Phagocytes congregated around a foreign body within a starfish, larva (from a drawing by Mechnikov)

dermal cells, i.e., derived from the mesoderm in the process of embryonic development (these include mesodermal cells which perform digestive functions in sponges and those which perform markedly different functions in the larvae of echinoderms and tunicates as well as in molluscs, worms and insects). In observing the transparent larvae of echinoderms (starfishes and holothurians) which are so easy to study, Mechnikov discovered that the mesodermal cells—phagocytes—enveloped and digested certain parts of the larval organs which had already served their purpose and were no longer needed (for instance, the ciliated band). Similar phenomena were observed in the complex process of metamorphosis in ascidians. His interpretation was the same as that given of the phenomena which his fellow-student Ganin had observed during metamorphosis in flies but which he had been unable to explain exhaustively. There remained only one logical step—and Mechnikov took it. He theorized that amoeba-like phagocytes digested not only certain parts of a given organism which have ceased to be serviceable but also all foreign matter which penetrated, one way or another, into the organism. These are his own words: "It is easy to prove that amoeboid cells are capable of enveloping and digesting (more or less completely) all extraneous matter." (*Ibid.*, p. 254.) He performed numerous and extremely varied experiments with transparent echinoderm larvae, introducing India ink, carmine granules, human red corpuscles and vegetable cells (bits of pea sprouts) into their bodies. The methods he used to introduce those substances into the larval body were different: in some cases the larvae swallowed the extraneous matter from the solution in which they lived; in others, the foreign matter was "offered" on the tip of an extremely thin glass tube; in still others, the grains were buried under their skins. But regardless of the path by which foreign matter entered the larval body, the amoeboid cells engulfed it, deposited it in their protoplasm and devoured it in such quantities that they became depots of India ink, dye, fat or protein granules. Occasionally, several cells united and produced a giant multinucleate cell—a plasmodium. In certain cases, particularly when particles of some indigestible substance, such as minute bits of glass, had entered a larva's body, the amoeboid cells surrounded them, holding them "captive" and preventing movement of the particles in the body. All these observations served Mechnikov as a basis for new and far-reaching conclusions.



A foreign body (glass tube) surrounded by phagocytes in the body of a sponge (from a drawing by Mechnikov)

How did these marvellous properties of mesodermal phagocytes arise and in what way were they preserved? To answer this question, Mechnikov reverted once more to his ideas concerning the origin of metazoans, which took final form in 1888. He maintained that, in the primitive ancestor of the metazoans, the amoeboid cells, whose function was digestion, formed the inner digestive layer—the phagocytoblast. In the course of evolution, the functions of the originally uniform cells of this layer, which could be called the mezoentoblast, were differentiated, part of the layer giving rise to the digestive tract as such, which, in lower animals, performs the function of intracellular and, in higher animals, extracellular, or coelomic, digestion. The other portion of the phagocytoblast also preserved the property of intracellular digestion; in the course of evolution it became the medial germ layer—the mesoderm. What was the significance of this property? Was it a mere "reminiscence" of an important evolutionary stage which, however, had long since been left behind? Perhaps it had been a necessary stage in the evolution of the animal kingdom but was of little importance in the life of the organism—just as many other stages which possess significance only in connection with the biogenic law—"ontogeny recapitulates phylogeny"?

Then Mechnikov presented an inspired solution of the problem: "The mesoderm ... has not lost its primary function, but has concentrated solely on *digesting harmful and useless substances*." (Author's italics. *Ibid.*, p. 267.) He was able to substantiate this thesis, thanks to his vast knowledge of biology and his evolutionary type of thinking. And, indeed, at the bottom of the zoological scale, where phagocytosis is the only method of nutrition—in protozoans and lower metazoans—it naturally performs the function of defence. Along with food, primitive animals may take in various harmful substances, including pathogenic micro-organisms, such as bacteria, moulds, and fungi, all of which occur so abundantly

in nature. These are digested together with food, but it is quite possible that, in the course of evolution, the cells enveloping and digesting food acquired the additional ability to destroy harmful substances or micro-organisms. Once this conjecture is accepted, an evolutionist cannot help taking the next logical step: the defensive function of phagocytosis, so advantageous in the struggle for existence, of necessity had to be preserved in certain groups of cells which arose from the primary phagocytoblast even after digestion in the intestinal tract had made intracellular digestion of food superfluous. Moreover, the defensive function of phagocytosis was strengthened and specialized. In Mechnikov's words, the amoeboid cells took on the "prophylactic function" of destroying unnecessary or harmful parts of the organism itself (atrophied larval organs in metamorphosis, moribund parts), as well as any injurious factor penetrating from without. These cells became very active, capable of discovering the enemy before it chanced to come their way. This activity manifested itself in a highly developed sensitivity to chemical irritation—chemotaxis—which enabled them to act in the presence of a foreign particle, in relatively quick amoeboid movements, and in the potency of the digestive enzymes contained within their protoplasm. That is how in the process of evolution, intracellular digestion of food, which has become unnecessary, gave rise to a new, biologically very important, attribute—the defence of the organism against harmful substances. This important property of mesodermal cells in metazoans is inherited from their protozoan ancestors while their morphogenetic properties are of secondary origin. As Mechnikov himself says: "Originally the mesoderm performed the role of engulfing and digesting food and ... its participation in the formation of tissues and organs developed later, as a secondary function." (*Ibid.*, p. 268.)

The conjecture about the defensive function of mesodermal cells, made on purely theoretical grounds, could be verified by experiment. One had only to introduce into a given organism a foreign body, not necessarily harmful, and watch the reaction of the amoeboid cells, observe whether they reacted to the intrusion, whether they could move to meet it and neutralize it.

This was the idea which struck Mechnikov on that December morning with which we began our story. He had thought of a simple and convincing experiment, consisting of thrusting rose thorns into the body of a starfish larva; this experiment supplied an equally simple and convincing answer—the amoeboid cells rushed from all parts of the larva's body to the thorn to protect the body from the intruder. But if the phagocytes were so active in defending the body against a relatively harmless agent, they should be a thousand times more active in defending it against noxious factors, primarily bacteria. Several months later, in the spring of 1883, Mechnikov wrote: "It seems likely that throughout the animal kingdom the food-enveloping and food-digesting functions of the wandering mesodermal cells serve to protect the body from bacteria." (*Ibid.*, p. 265.) This idea was the foundation for all the varied researches necessary to prove the correctness of the idea possessing Mechnikov.

In becoming a pathologist, Mechnikov did not forsake zoology, or rather, biology. He applied to pathology—we should say, to medicine—those ideas which he professed in biology (above all, the evolutionary, comparative historical method). It was the absence of this method in contemporary medicine which prevented it from being a biological science. Throughout his lifetime Mechnikov strove to achieve a synthesis, a fruitful co-operation between biology and medicine—a feeling he clearly expressed in the conclusion of his *Investigation of Intracellular Digestion in Invertebrates* written at the friction between two seemingly different but in reality closely connected periods of his scientific career. He wrote: "The great advance in

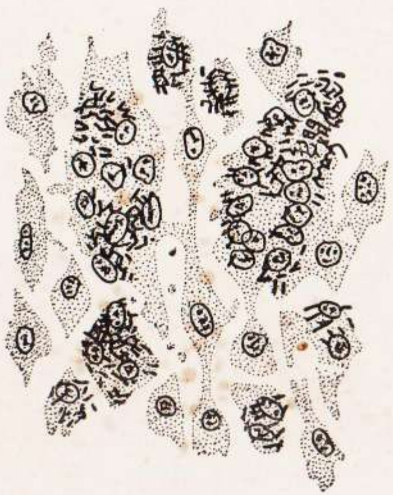
pathology made in recent years, will certainly influence zoology which, once it has adopted the evolutionary standpoint, will in turn facilitate the solution of medical problems by means of comparative pathology." (*Ibid.*, p. 270.)

GENERAL APPLICATION OF THE PHAGOCYTIC THEORY. BIOLOGICAL DOCTRINE OF INFLAMMATION

Mechnikov took his first step in pathology, accomplishing this sharp turn in his work with his accustomed impulsiveness. So far it was a miraculous "revelation," a prescience of future discoveries, but no actual knowledge based on solid facts. The struggle in behalf of the phagocytic theory had barely begun. Mechnikov perceived that a vast ocean of work on different aspects of the new problem confronted him. It is our hope that the reader will forgive us if we do not adhere to the chronological principle in listing his works; it is our aim to show the natural and logical development of the scientist's idea, which did not always coincide with the sequence of his research, determined as it was by various causes, sometimes of secondary importance.

Mechnikov felt that the first thing to do was to provide a general interpretation of the wonder he had seen in Messina.

For all their breath-taking interest, the observations he made on the amoeboid cells in the starfish larva would have remained a curious zoological phenomenon, an individual fact or even a downright mistake, had they not been proven by a number of other, most varied, observations. The most important thing for Mechnikov was to prove beyond all doubt that the function these cells performed *was* that of protecting the body from its numerous enemies. Some time was to elapse before he was eventually able to do so.



Human tuberculosis bacilli phagocytosed by macrophages of a pigeon (from a drawing by Mechnikov)

Mechnikov's friend, Kovalevsky, had in his aquarium in Odessa minute transparent crustaceans of the genus Daphnia, very common in all fresh-water reservoirs, ranging from big lakes to small pools. The Daphnias were attacked by the needle-like spores of the *Monospora bicuspidata* fungus, which penetrated their bodies and germinated there. The entire course of the disease could be easily observed owing to the Daphnia's transparency. Mechnikov saw the amoeboid cells congregate at the spots where the spores had penetrated, envelop and devour them. This was another proof of the defensive role of the phagocytes. His observations on the more or less acute course of the disease (depending on the number of the spores that had been able to penetrate into the body), as well as his infecting the Daphnias with the fungus artificially, enabled Mechnikov to follow in detail all the stages of the dramatic encounter between phagocytes and spores which took place under his microscope. When the phagocytes were sufficiently vigorous, the spores were "phagocytosed," the body was freed from the fungus, the animal got well and resumed its characteristic leaps in the water; but in cases where the wandering cells were weak, the spores proliferated rapidly, the phagocytes were unable to cope with them and the Daphnia died. The observations were almost as clear as a diagram, revealing

the events taking place in a diseased organism and proving the defensive function of the phagocytes. The most varied animals, including vertebrates, might present the same picture; the universal occurrence of phagocytosis is proof of the major biological significance of this phenomenon.

Next, Mechnikov wanted to find out what particular cells performed the phagocytic function. At first, he thought this function was performed by mobile mesodermal elements—blood cells in vertebrates and amoeboid cells of the intercellular fluid in invertebrates. Gradually more and more data became available from which it became evident that phagocytosis was much more widespread than had hitherto been supposed. It has been previously mentioned that, in the metamorphosis frequently occurring in invertebrates and even in some vertebrates, larval organs disappear and are replaced by organs peculiar to the adult form, for instance, the tadpole, in which the mouth, gills, enteron and tail either disappear or undergo a complete change. Mechnikov carefully studied the morphology of frog metamorphosis, discovering that the organs which have served their purpose were digested by phagocytes. A few years later (in 1888), A. Kovalevsky confirmed his observations on fly metamorphosis, during which larval tissues are almost completely destroyed and the adult organs are formed anew. Both he and Mechnikov noted that phagocytosis was effected not only by the amoeboid cells derived from the blood. Local amoeboid cells derived from connective tissue, and even simplified cells of a specialized (e.g., muscle) tissue acquiring the property of phagocytosis, also participated in the process. This constituted an entirely new aspect of the original idea, serving to throw additional light on the biological role of phagocytosis.

* * *

Mechnikov noted a certain similarity between what he had observed in Messina and exudation accompanying inflammation in higher animals. This idea brought him ever closer to medicine, attracting his attention to a familiar diseased condition—inflammation—whose classic five characteristics—*tumor, rubor, calor, dolor cum functio laesa*—had been memorized by generations of medical students all over the world. Although long an object of detailed study, the cause and biological significance of inflammation was unknown to medicine. Some scientists, for example, the great German pathologist Virchow, attributed the cause of inflammation to disturbed nutrition and intensified cellular proliferation due to injury inflicted by a pathological agent, considering *tumor*, an agglomeration of cells, to be the cardinal sign of inflammation. Others (Cohnheim and Samuel) held that inflammation was caused by lesions in the walls of blood vessels, accompanied by the exudation of serum and blood corpuscles which collected around the diseased vessels forming the characteristic swelling. True, there are always a large number of leucocytes to be found surrounding an inflammatory focus, some of them containing bacteria specific for a given disease. But no one was able to present a correct interpretation of the phenomena observed. Thus, Cohnheim thought that the leucocytes, migrating through the porous walls of the vessels, formed pus around the foreign body, whose pressure on the inflamed spot caused pain. He, therefore, proposed to search for a means to prevent the leucocytes from migrating through the walls of the blood vessels. Even the great Koch himself was unable to perceive the true state of affairs contending that the leucocytes served as food for bacteria and so the bacteria penetrated into the protoplasm of the white corpuscles.

It was Mechnikov who correctly interpreted inflammation as a defensive reaction of the body against infection, or for that matter, against any foreign substance present in the body. What was it which enabled him to solve this old and extremely complicated problem which had presented a challenge to physicians almost since the days of Hippocrates? His success was due mainly to his biological approach to the problem of inflammation. Mechnikov was something more than only a biologist; he was an evolutionary biologist, a true devotee of Darwin's doctrine, capable of applying its principles to the problems he studied. In the preface to the Russian edition of his classic *Comparative Pathology of Inflammation*, Mechnikov says: "The principal aim of my work is to establish a lasting connection between pathology and zoology, or rather, biology in general.... Just as in former days, comparative anatomy was limited to the study of man and higher animals, medicine, up to now, has persistently ignored all pathological phenomena taking place in lower animals. And yet, these same animals, presenting the simplest and most primitive conditions, provide a key to the understanding of the complicated pathological phenomena encompassed by the field of medicine." (*Comparative Pathology of Inflammation*, Medgiz, 1947, p. 3.)

Mechnikov was the founder of a new branch of zoology—comparative pathology—whose significance he illustrated by one of the oldest and most complex problems of medicine—that of inflammation. He drew up a list of questions dealing with inflammation, to which comparative pathology was to find the answers. Is inflammation in lower vertebrates (lancelet) and invertebrates caused by the same factors operating in man and higher vertebrates? Is a vascular system an essential condition for the manifestation of inflammation or it can occur in animals which have no blood vessels? What is the role of the nervous system in the latter event? Must an animal possess a certain number of differentiated organs for inflammation to develop or it may consist merely of a conglomerate of non-differentiated cells? Do vegetable forms exhibit a reaction analogous to inflammation? Can inflammation occur in unicellular organisms?

Comparative Pathology of Inflammation was Mechnikov's answer to these questions. He arrived at the conclusion that the chief defensive apparatus in amoebae, flagellates, and infusoria consists of intracellular digestion, by means of which parasitic organisms are destroyed and their remains excreted from the host's body. The digestion of parasites results in the host's recovery. In myxomycetes (slime moulds), Mechnikov studied in great detail one characteristic of inflammation—great sensitivity to chemical action (chemotaxis)—which enables the mould to move away from the source of harmful influences. A curious fact about these peculiar organisms is that they are able to rid themselves of parts of the body which are moribund as a result of injury or which envelop a foreign body (for instance, a glass tube). A modification of this property manifests itself in higher animals in the inflammatory reaction. Mechnikov then took the simplest of metazoans—sponges—and showed that, owing to differentiation of functions and specialization of cells, intracellular digestion became the specific property of amoeboid cells. It is these very cells which react to the entrance of a foreign body, envelop it and, whenever possible, digest it. Sometimes such cells congregate in large masses around some living or non-living matter and encase it. Mechnikov observed similar reaction to the introduction of foreign substances or of micro-organisms in medusae, starfish (the experiment which led to the discovery of phagocytosis), worms and other invertebrates. Roundworms which have no wandering cells, or phagocytes, do not show this typical reaction when solid particles, parasites and the like enter their bodies.

All the above forms have either no vascular system or a very primitive one (ringworms), consisting of a coelom filled with a coloured fluid containing haemoglobin and a few blood cells called amoebocytes. The vessels of higher forms such as arthropods, molluscs and Protochordata, contain a larger number of blood cells resembling

the leucocytes of higher vertebrates and differing from them only in some structural details. As early as 1862, scientists proved that these cells were phagocytes by introducing harmless dyes into organisms. Mechnikov cited numerous examples showing that when the body was injured or foreign agents penetrated into it, phagocytes gathered in large masses, surrounding the pathogenic factor which was then ingested and destroyed.

Mechnikov studied white axolotl as an example of inflammation in amphibians. Step by step he observed how in response to irritations—burns, pricking with a needle dipped in carmine or indigo—connective tissue cells became mobile, moving towards the injured spot, devouring the remains of injured cells, dye granules, etc. Blood vessels underwent no change, exhibited no hyperaemia, and the leucocytes took no part in the inflammatory reaction. Such was the case in young amphibian larvae; but in the older larvae of triton and axolotl with numerous blood vessels from which leucocytes can migrate, the response to irritation was more complicated. Here inflammation presented its most complicated classic form—the flow of blood was impeded, the leucocytes grouped along the periphery of the capillaries and migrated through their walls. The picture observed was in no way different from inflammation occurring in higher animals and in man.

In describing inflammation as a defensive reaction of the body, Mechnikov pointed out that not every defensive reaction is inflammation. Inflammation is characterized by the participation of mesodermal cell elements whose phagocytic and digestive property has acquired a pronouncedly defensive significance. Wherever this phagocytic reaction takes place, there is inflammation, no matter what kind of animal exhibits it and how complex or simple the reaction is. "It is quite clear," Mechnikov says, "that inflammation in vertebrates, in which the phagocytes leave the vascular system and rush to the invader, differs merely quantitatively from similar phenomena in invertebrates. Consequently, it should be regarded as the organism's reaction to harmful influences . . . the main source of inflammation being the phagocytic reaction of the living organism. All the rest are mere accessories of this phenomenon and can be reduced to adaptations facilitating the flow of phagocytes to the injured area. (*Comparative Pathology of Inflammation*, p. 107.)

Since the main characteristic of inflammation is phagocytosis, it follows that the characteristics of inflammation in vertebrates (distension of blood vessels, migration of leucocytes and their congregation about the source of irritation) should be regarded as manifestations of the defensive phagocytic reaction.

Seen in the light of Mechnikov's works, inflammation, which had long been regarded as a manifestation of disease, serving to aggravate its course, was found to be a manifestation of biological self-defence of the organism. This thesis was destined to play an extremely important role in medicine. Where inflammation is weak, where there is no phagocytic reaction, the disease progresses rapidly to a lethal outcome. Below we shall cite a number of concrete examples from Mechnikov's works to prove this point.

Mechnikov attached a great deal of importance to the vascular system which enables the phagocytes to approach the injured area, thereby facilitating the reaction of inflammation. It is for this reason that this reaction is more pronounced in higher vertebrates possessing a well-developed circulatory system capable of quickly mobilizing the organism's defensive forces.

Mechnikov then gives a detailed analysis of the cellular elements participating in the reaction of inflammation, above all leucocytes, and points out that a characteristic structural feature of some of the leucocytes—the split nucleus—is probably connected with their ability to penetrate the capillary walls.

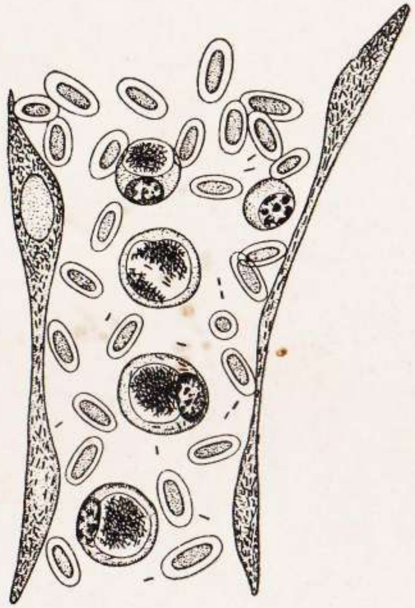
* * *

Mechnikov noticed that leucocytes were not the only participants in the inflammatory reaction. In studying the different morphological elements of the inflammatory exudate forming around the foreign body, he repeatedly observed large cells containing a dark round nucleus and amoeboid pseudopodia, very sensitive to chemical irritants. He regarded these cells, too, as phagocytic, whose function was the disposal of the remains of decomposed tissues, dead cells, etc. In this connection, he mentioned the resorption of parts of an organism which are no longer needed—as occurs during metamorphosis. As we have seen, this function is discharged by non-mobile tissue cells and by simplified specialized elements. He established that the chief "duty" of the fixed cells consisted in digesting injured or dead tissue elements and the "corpses" of leucocytes. Despite the similarity of their functions, different categories of cells are essentially dissimilar with respect to their morphology and to their other properties. Because of this, Mechnikov introduced two new terms: *microphages* (for the phagocytic blood cells possessing a segmented nucleus) and *macrophages* (for big mononuclear blood cells and for fixed—or originally fixed—cells of the connective tissue and of vessels). The first of these terms was not accepted by all, but the second has been incorporated into the vocabulary of modern morphology.

* * *

Further progress in the study of the functions of the body's non-mobile defensive elements, including clarification of some aspects of the phagocytic theory, was the work of the Russian pathologist, Vladimir Vysokovich (1854-1912).

A graduate of Kharkov University and a pupil of the famous microbiologist L. Tsenkovsky, Vysokovich was well versed in the new and developing science of bacteriology, but as a pathologist, he was interested not in the pathogenic agent but in the infection—the path by which it enters the organism, the channels along which it spreads, the influence it exercises on the organism and the organism's defences against it. In 1886, he wrote a classic work entitled *The Fate of Micro-Organisms Introduced into the Blood of Homoiothermic Animals.* In his experiments, Vysokovich introduced mould fungi and bacteria into the blood stream of rabbits—agents which were harmless or injurious (pathogenic) to the given animal. He observed that, while harmless organisms were digested by the leucocytes in the rabbit's blood, pathogenic microbes disappeared from the blood. By means of microscopic studies, he discovered large numbers of these bacteria not only within the macrophages described by Mechnikov, but also within the cells forming the walls of small blood vessels in the spleen, lymphatic nodules, bone marrow and liver. Vysokovich confirmed Mechnikov's observations regarding the role of non-mobile elements of connective tissue in phagocytosis and supplemented his data with the discovery of the important role played in this process by the endothelial cells forming the walls of blood vessels. Vysokovich pursued his experiments further and discovered that smears from liver, spleen and bone-marrow tissues contained live bacteria capable of reproducing. Under the microscope, the phagocytes were seen to contain proliferating bacteria the lymphatic nodules teemed with bacteria which reappeared in the blood stream. Vysokovich concluded that pathogenic microbes (and no others) not only remain alive in the cells of the blood-vessel wall but even find the conditions existing there conducive to proliferation. These observations illustrate the fact that a simplified interpretation of phagocytosis was not acceptable to Vysokovich; he understood that an organism's defensive mechanism was not confined to one property alone and that the mechanism did not always ensure a complete destruction of bacteria. He made his viewpoint clear in an article entitled "The Study of Anthrax," published in *Vrach (Physician)* in 1891: "I must add that whereas, in general, I believe in the phagocytic property of the cells of certain kinds of connective tissue . . . I am far from regarding the enveloping of bacteria by these cells as the only method by which the body combats infection. Bacteria can perish quickly in blood and tissue fluids without being ingested but, when ingested, they can overpower the cell, kill it, feed and proliferate at its expense—which is what happens when virulent anthrax bacilli are introduced directly into the blood stream." It would seem at first glance that there was a marked difference between this viewpoint and the one advocated by Mechnikov, and as early as the eighties, the two scientists were believed to be at loggerheads ideologically. But actually, for several years, Mechnikov and Vysokovich carried on fruitful and amicable discussions. Mechnikov did not think that all bacteria entering the body were necessarily destroyed; he knew that many of them secrete special substances which incapacitate phagocytes. Even when engulfed by phagocytes, bacteria do not always perish. Occasionally, within the phagocytes, the bacteria will find conditions favourable to life and proliferation. In



Part of a pigeon's hepatic vein whose endothelial cells have phagocytosed the microbe of pig erysipelas (the Vysokovich effect) his article "The Relation of Phagocytes to Anthrax Bacilli," published seven years earlier than Vysokovich's article, Mechnikov says: "Even if we may assume the destruction of part or all of the bacteria in case of a bacterial disease, we must grant *a priori* that there are some pathogenic bacteria which, engulfed by phagocytes, can withstand their destructive action and instead of perishing, develop and proliferate within their bodies.... In a similar manner to the way in which many worms may become parasitic in the alimentary canal of frogs or some other animals, some bacteria may—I mean should—become adapted to the conditions prevailing inside the phagocytes and turn into the parasites instead of the prey of the phagocytes." It may be seen from this that Mechnikov's and Vysokovich's views differed *not* in their appraisal of phagocytes and their specific activity, but as regards the role of the leucocytes in defending the body from infection. Mechnikov held that the mobile cells of blood (the microphages) played the most important part in combating pathogenic microbes. Vysokovich denied their role in the fight against pathogenic bacteria and attributed much greater importance to the non-mobile elements of the connective tissue. He said: "True, we have as yet very inadequate factual data enabling us to comprehend the particular phenomena attendant on the development of disease, but those we do have are sufficient to make us consider the cellular elements of the fixed connective tissue and not the white blood corpuscles as the main infection-resisting force of the body. This is the chief point of disagreement between Professor Mechnikov and myself." (*The Cause of Suppuration*, 1887.) Vysokovich's viewpoint was better substantiated. He attached particular importance to the primary cells of the connective tissue found in all multicellular animals, whereas blood cells capable of phagocytosis are encountered in vertebrates alone. Moreover, he showed that the ability to engulf and digest highly-dispersed substances—those generated

within the organism and those occurring externally—is a specific property of connective cells.

The truth emerged out of dispute and reciprocal correction; in this way was born a fruitful theory of modern medicine—the macrophagic-endothelial system of Mechnikov and Vysokovich. This is really the correct term for describing the protective system of the organism now rather incorrectly called the reticulo-endothelial. In addition, elaboration of this system was the work of both Russian (including Academicians A. Bogomolets and N. Anichkov) and foreign scientists. It was discovered that this system, spread throughout the entire body, plays an important part both in the protection of the body from infection and in metabolism of proteins and fat-like substances.

Recently, the doctrine of the macrophagic system has been enriched by the work of B. Kedrovsky, a Soviet cytologist. Making use of the ideas of Mechnikov and Vysokovich, he has come to the opinion that the chief duty of the macrophages is to digest proteins. According to his theory, an excess of proteins enters the blood and is carried to other cells of the body. This serves to explain why macrophagic tissue is so abundant, making up nearly 30 per cent of the body's soft tissue. Pursuing his idea further, Kedrovsky pointed out that when the quantity of substances coming from the external world is too large, such substances are deposited in the macrophages. In the course of evolution, macrophages have acquired the ability to engulf and digest not only food but all foreign particles, living and non-living, of a specific size. This new property determined the appearance in them of a new, defensive function. And finally, as the ultimate stage in the evolution of this function, the ability to unite chemically with foreign and often harmful substances developed, and antibodies were produced.

Some scientists, Academician Bogomolets, for example, were apt to overestimate the importance of the macrophagic system in the organism's life, attributing to it a leading role in various processes and considering the stimulation of this system a panacea for each and every disease. Such a viewpoint is certainly quite erroneous, since it ignores the role of the central nervous system in the complex interrelations existing among the internal humoral factors which unify the whole of the organism.

Mechnikov's data on the fixed cells of the connective tissue are of great significance. The joint participation of blood cells—leucocytes—and connective-tissue cells in the defensive reaction of inflammation is evidence that the two cell groups are closely related. From this it follows that blood and connective tissue (particularly loose connective tissue) should be regarded as a single internal medium in the organism, showing similar (and yet specific) reactions to the influence of external factors. The close similarity between blood and tissue-cell forms may be seen from the fact that both of them are called upon to participate in the first stage of inflammatory reaction—in enveloping and (whenever possible) devouring the irritant. This close similarity may be observed in their further destinies: when inflammation has subsided, tissue cells may enter the blood stream as leucocytes (usually as monocytes) or blood cells may settle in the connective tissue and become macrophages, i.e., wandering cells become fixed.

Thus the consistent application of the comparative-biological method enabled Mechnikov not only to understand a very complex pathological phenomenon (inflammation), but to elucidate a number of other important problems in biology and medicine.

* * *

The above may create the impression that Mechnikov considered the phagocytic reaction of mesodermal elements to be the sole defensive reaction, wholly independent of other regulating forces of the body. Such was not the case. Mechnikov understood perfectly well that the body as a whole could not but influence the course of the

phagocytic reaction and that this influence was exercised through the medium of the nervous system. This is what he wrote in discussing the theory of inflammation of Kuss and Landerer: "The drawback of this theory lies in its disregard of nervous influences." (*Comparative Pathology of Inflammation*, 1947, p. 147.) He went on to describe in detail the experiments of Samuel, Roger and Danilevsky, who demonstrated the marked influence the nervous system exercises on the course of inflammation. These research workers established that by affecting various parts of the nervous system, such as the sympathetic, sensory nerves, etc., in different ways, they were able to alter the course of the inflammatory reaction, accelerating or retarding it, expanding or limiting the area over which it spread. These data show that the more complex the organism is, the more pronounced is the role of the nervous system in the process of inflammation. Mechnikov was prompted to mention this in his most complete definition of inflammation: "In its entirety, inflammation should be regarded as a phagocytic reaction of an organism in response to irritating agents, sometimes performed by mobile phagocytes alone and, at other times, carried out jointly with vascular phagocytes or with the nervous system." (*Ibid.*, p. 183.)

Mechnikov attached some importance to the role played by the tactile and chemotaxic sensitivity of the phagocytes in the process of inflammation. This sensitivity establishes direct and close relationships among the different elements of the phagocytic system (in vertebrates, where it is most highly developed); furthermore, it provides for instantaneous and unfailing reaction to outside irritants. In Mechnikov's words: "This reaction is accomplished with the aid of living ties existing among connective-tissue cells, endothelial elements and leucocytes, and forming an uninterrupted chain which plays the principal role in inflammation occurring in vertebrates." (*Ibid.*, p. 185.)

Mechnikov's biological theory of inflammation has repeatedly been regarded as "vitalistic." Accusations of "vitalism" were based on Mechnikov's manner of expressing his ideas, which sometimes smacked of anthropomorphism; for instance, "The mesodermal cells are capable of a certain protozoic *spiritual* [my italics.—*S.Z.*] activity." (*Intracellular Digestion in Invertebrates*, 1950, p. 267.) This and similar unhappy expressions supplied sufficient ground for accusing him of idealism and vitalism.

Mechnikov himself protested strenuously against this accusation. He quotes Fraenkel's words (*Grundriss der Bacterienkunde*, 1890): "The theory of phagocytosis assumes that the protoplasm of leucocytes possesses astonishing properties; quasi-real sensations, thoughts and actions, a kind of psychic perception—are attributed to it," as an example of "the most sincere" conviction in the vitalistic nature of his views. Mechnikov says: "As to attributing to leucocytes the properties of thinking and volition, for which Mr. Fraenkel reproaches me, it is clear that there is no question about that.... Vitalism and animism unjustly ascribed to the theory of phagocytosis should be imputed to my adversaries who hold that psychic acts of higher animals are something entirely different from the simplest phenomena occurring in lower beings." (*Comparative Pathology of Inflammation*, 1947, p. 186.)

Mechnikov likewise refuted the charge of teleology. He pointed out that inflammatory reaction was based on the law of evolution, on useful properties being retained in the course of natural selection, handed down to the offspring, becoming more deeply rooted. At the same time, there is no doubt that this adaptive reaction is far from perfect. As Mechnikov says: "The phagocytic apparatus has not yet reached the final stage in its evolution; it is still on the road to perfection." This explains why phagocytes are sometimes unable to perform their task and, as Mechnikov puts it, "run away from the enemy" or are overcome by the pathogenic agent. Mechnikov considered

the comparative biological method effective in the study of other pathological conditions, such as fever, the growth of tumours, atrophies, etc., and concluded his book, which was actually a course of lectures, just as he had started it, with an appeal to scientists to develop comparative pathology which would benefit both biology and medicine.

We have dwelt at such length on this remarkable work on inflammation, because it is especially characteristic of the new period in Mechnikov's career when his broad biological approach, wide erudition, clarity of thought, and keen interest in preserving the health and happiness of mankind became particularly manifest. And yet it was but a link in the chain of his work which, beginning with comparative embryology, enticed him further into the thick of pathological and medical problems.

IMMUNITY IN INFECTIOUS DISEASES. THEORY OF CELLULAR IMMUNITY

Mechnikov blazed a new road for research workers who came after him, but at the same time he himself continued to work in this new and entrancing sphere of science. While pursuing his study of phagocytosis, he observed that an animal's immunity to a given pathogenic agent was very intimately connected with the intensity of the phagocytic reaction.

To the question—What is immunity?—Mechnikov gave the following answer: "Immunity to infectious diseases should be understood as resistance of the organism to the microbes that cause the disease." (*Immunity in Infectious Diseases*, 1951, pp. 19-20.) On the basis of the "biological theory of inflammation," Mechnikov thought that here, too, the active mesodermal elements, phagocytes, must play the leading role.

A graphic example of this activity is supplied by the fate of anthrax bacilli introduced into the body of a frog or guinea-pig. The phagocytes in the body of the frog devour the anthrax bacteria, and frogs never develop the disease—they are immune to anthrax. In the blood of the guinea-pig, on the contrary, anthrax bacilli are not devoured by the phagocytes, and the guinea-pigs succumb to the disease.

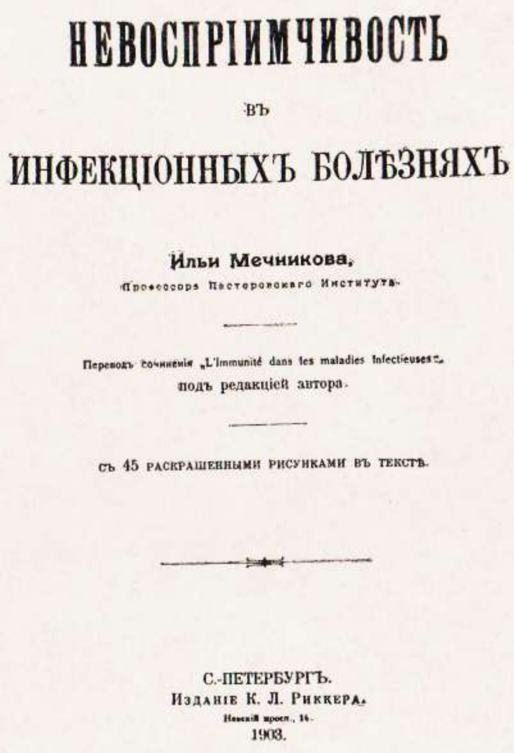
The normally vigorous reaction of phagocytosis can, however, be weakened. In that event, animals usually immune to the disease will contract it. Chickens and pigeons are immune to anthrax, because their leucocytes, like those in the frogs, actively destroy anthrax bacilli. But if the phagocytic activity of the leucocytes is weakened, say, by cooling the birds, the fatal disease develops in them, too.

Conversely, immunity arises when there is an intensification of the phagocytic reaction. If a rabbit is inoculated with an active culture of anthrax bacillus, it rapidly dies, and only an insignificant number of leucocytes can be found at the inoculation site. But if a rabbit is inoculated with a weakened culture of the same bacillus, it will survive; there will be a mass of leucocytes at the inoculation site and intensive phagocytosis of the germs.

This shows that the devouring of microbes in an immune organism is a particular instance of the activity of phagocytes. If this be the case, immunity should be studied by the comparative biological method as a historically evolved property of living organisms, as part of *digestion in general.* Mechnikov, accordingly, became absorbed in the study of the new problem.

* * *

At that time, the problem of immunity to infections was attracting the attention of scientists and practising physicians alike. Natural (inborn) and acquired (developing after the recovery from a specific disease) immunity had been generally known for a long time. Pasteur discovered artificial immunity when, in 1880, he inocu-



НЕВОСПРІИМЧИВОСТЬ

ВЪ

ИНФЕКЦІОННЫХЪ БОЛѢЗНЯХЪ

Ильи Мечникова,

Профессора Пастеровскаго Института.

Переводъ сочиненія „L'Immunité dans les maladies Infectieuses",

подъ редакціей автора.

съ 45 раскрашенными рисунками въ текстѣ.

С.-ПЕТЕРБУРГЪ.

Изданіе К. Л. Риккера.

Невскій просп., 14.

1903.

Title page of the first Russian edition
of Mechnikov's *Immunity in Infectious Diseases*

lated chickens with a weakened growth of chicken-cholera bacteria (vaccine), thus enabling them to survive when they were subsequently infected with a virulent culture of the same bacteria. Medicine was faced with a very important task—to elaborate preventive measures to control a number of infectious diseases which customarily took a heavy toll of life, particularly among the poorer strata of people. And yet this highly important branch of medicine lacked theory. Mechnikov devoted himself to providing this theoretical basis. He studied the phenomenon of immunity beginning with the amoeba and ending with the higher animals and man. He studied the adaptations possessed by various organisms enabling them to invade their hosts, and the means by which the latter protect themselves from the parasites. Approached from this broad standpoint, infection and immunity (whether natural or acquired) are merely special instances of a fundamental problem of general biology, which had attracted Mechnikov at the dawn of his career—the problem of parasitism.

In this way, a new doctrine arose, unifying biology and medicine—the theory of cellular immunity. As before, phagocytosis was assigned the leading role in this most important defensive reaction of the body. "Phagocytosis alone is the permanent element in both natural and acquired immunity. The universal occurrence and significance of this factor are now beyond dispute. It has been proved convincingly that phagocytes are sensitive cells reacting to organized and non-organized injurious agents. . . ." (*Immunity in Infectious Diseases*, p. 461.) We shall see, however, that at that time, Mechnikov no longer considered intracellular digestion the only method of establishing immunity to a specific disease. He realized that the substances produced by phagocytes played a significant role. He stated that phagocytes (in higher animals, at least) were not absolutely autonomous and perfectly independent of the body's regulating forces. On the

contrary, he attributed to these influences, particularly to the activity of the nervous system, a decisive part in the creation of the organism's immunity to infection.

On page 85 of the work to which we refer, he wrote: "In studying the general properties of intracellular and secretory digestion, we see that chemical processes in both are influenced by the living parts of the body. In lower animals, the chemical side of digestion is governed by the protoplasm in the amoeboid cells, and, in higher animals, this function is discharged by a very complex mechanism in which the nervous system plays the dominant part." He further pointed out that the activity of phagocytes was influenced directly by environment. Phagocytes were able to carry out their task owing to their exceptional sensitivity—a circumstance already mentioned. But this sensitivity was not constant. When a pathogenic agent (for instance, a microbe) entered the body, the metabolic process going on in the phagocytes changed, their activity increased, and, as new particles of the micro-organisms continued to invade the body, they were destroyed with particular intensity. Mechnikov thought that this provided the key to the specific nature of immunity which is so astonishing in this phenomenon. Immunity enables the organism to survive in spite of invasion by pathogenic agents, and, consequently, it is the sensitivity of the phagocytes which, in the final analysis, ensures the organism's adaptability. These new horizons alured Mechnikov irresistibly.

The scepticism that greeted the appearance of his theory of phagocytosis aroused the fighter in him. His fiery temperament urged him, embryologist that he was, to rush into the thick of the burning practical problems of medicine. Another characteristic of Mechnikov's that stood out prominently at that period was his humanism, a desire to do his best to ease the fate of suffering mankind.

In order to better understand the reasons which caused Mechnikov to start in a new sphere of science (a turn which, although conditioned by the consistent evolution of his scientific thought, still seems somewhat unexpected), it would be well to acquaint ourselves with the story of his life in those and following years.

MECHNIKOV'S WORK IN THE FIELD OF APPLIED ZOOLOGY. FOUNDING OF A BACTERIOLOGICAL STATION IN ODESSA. MECHNIKOV LEAVES RUSSIA AND BEGINS WORK AT THE PASTEUR INSTITUTE (1883-88)

While working at Odessa University in the late seventies, Mechnikov expressed interest in practical problems but these were as yet far removed from medicine. His active nature prompted him to put every theoretical premise to a practical test, the most reliable criterion of truth. This was the case, for instance, with his views on Darwinism.

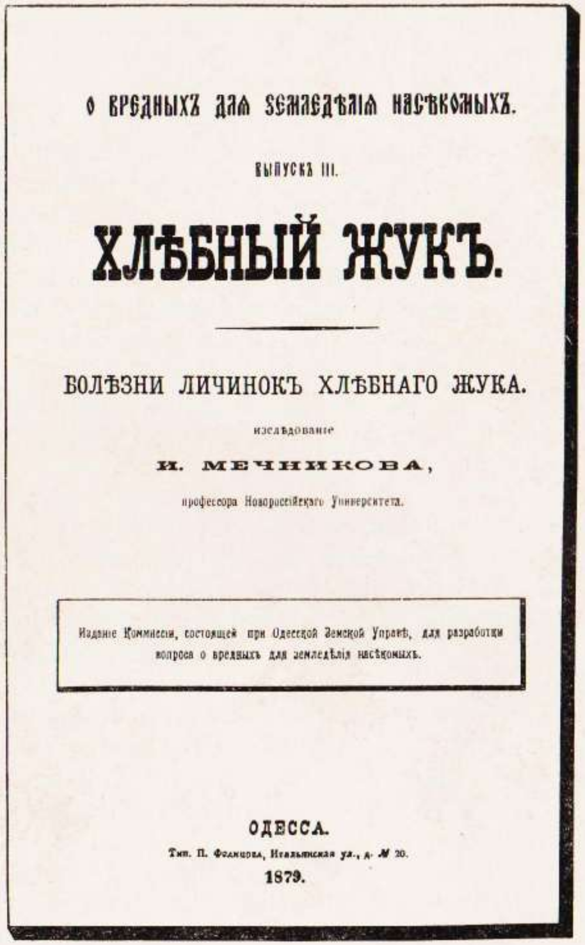
His conviction that inter-species struggle was a fundamental factor of evolution made Mechnikov consider utilizing this biological phenomenon in the interests of mankind.

He asked himself whether it was possible to make use of inter-species struggle in order to destroy harmful animals. In the late seventies, when he was only a zoologist, Mechnikov tried to approach from a purely biological standpoint an important economic problem—the control of agricultural pests, which in those years (and even much later) caused great damage to agriculture in the south of Russia. The chance observation of a dead fly with mould growing on it suggested to him that it might be possible to fight injurious insects by infecting them with micro-organisms. In various books, he read that insects were subject to various epidemic diseases. Thus in the sixties, Keppen, a well-known naturalist, observed an epidemic in the Crimea, which broke out among cockroaches belonging to the Orthoptera. Insects were found to be affected most often with a fungus germinating and growing on their bodies and imparting to the insect the shape of a lozenge. The fungus, known to naturalists since the thirties, was called muscardine (Fr. *muscardin* "a musk-scented lozenge"). In 1878, Mechnikov began waging a biological fight against injurious insects such as *anisoplia austriaca* beetles and beet weevils infesting cereal crops and sugar-beet plantations, the staple culture grown in those days in the south of Russia. He established contact with the Entomological Commission under the Zemstvo and in September 1878, reported on epidemic diseases of the larvae of agricultural pests at a congress of agriculturists. That same autumn, he began experiments the results of which were summed up in a booklet entitled *Anisoplia Austriaca—Diseases Affecting Its Larvae* published by the Entomological Commission under the Odessa Zemstvo Administration in 1878 as No. 111 in the series *Agricultural Pests*. Mechnikov had discovered that the larvae of the beetle were affected by three diseases: a fungous disease caused by green muscardine (so named on account of its green threads), a bacterial infection by Cornel bodies (vibrios which are generally present in the blood), and a parasitic disease caused by the thread-like larvae of the *Leptodera* worm. Of these, muscardine was the most important, because if the disease were to spread, an enormous number of beetles would be destroyed. Mechnikov, however, pointed out that spontaneous infection with the fungus (which he described in detail and proposed to name *Entomophtora anisopliae*) would hardly be of practical significance, as the epidemic spread slowly and this slow progress might cause immunity in the insects. He, therefore, started experiments on infecting the insects artificially with the fungus. He gave directions concerning the methods of spreading the fungus infection and insisted on founding nurseries in which to culture the fungus on a wide scale. He considered this to be the first step in a long series of research on different pathogenic agents—for instance, the myxosporidian parasite causing pebrine in insects—and on the control methods to be employed against different agricultural pests. Beet weevil and particularly phylloxera causing enormous damage to wine grapes, were considered especially dangerous. What is of interest here is his posing of the problem of biological measures to combat agricultural pests. Mechnikov expressed his views in the following way: "In studying injurious insects, particular attention should be paid to diseases to which they are subject, since the lower forms causing these diseases are the most potent force capable of eliminating the insects. These parasitic organisms should be our strongest allies in destroying animals harmful to man; that is why it is necessary to encourage in every way the spread of the former."

Many progressive biologists of the time, even those who were engaged in purely theoretical research, were eager to apply their knowledge to practical purposes. Thus, in 1881, Kovalevsky worked on the chemical and biological (utilizing muscardine) methods of combating phylloxera. The botanist L. Tsenkovsky devoted the last years of his life to work at the Kharkov Zemstvo where he applied the data accumulated by agricultural microbiology to controlling pests. Tsenkovsky even came to Odessa (probably in 1886 or 1887) to discuss this problem with Mechnikov and to acquaint himself with the new methods.

From the above examples, it is clear that progressive Russian scientists have always—even during the years of reaction—been eager to help society with their knowledge and experience.

To return to Mechnikov and his work in the sphere of biological methods of controlling agricultural pests. In 1879 and the following year, he conducted laboratory experiments, infecting beet weevil with muscardine. He obtained encouraging results and transferred his ex-



О ВРЕДНЫХЪ ДЛЯ ЗЕМЛЕДѢЛІЯ НАСѢКОМЫХЪ.

ВЫПУСКЪ III.

ХЛѢБНЫЙ ЖУКЪ.

БОЛѢЗНИ ЛИЧИНОКЪ ХЛѢБНАГО ЖУКА.

изслѣдованіе

И. МЕЧНИКОВА,

профессора Новороссійскаго Университета.

Изданіе Коммиссіи, состоящей при Одесской Земской Управѣ, для разработки
вопроса о вредныхъ для земледѣлія насѣкомыхъ.

ОДЕССА.
Тип. П. Францова, Итальянская ул., д. № 20.
1879.

Title page of Mechnikov's booklet *Anisoplia Austriaca—Diseases Affecting Its Larvae* (1879) periments to the field, entrusting A. Krasilshchikov, a young entomologist, with continuing his work on the sugar-beet plantations. Here, too, things went well and in 1883-84, large quantities of muscardine cultures were obtained and methods for its utilization improved. And that was the end of it! One of the obstacles in the way of further development of the biological method was a crisis in the sugar industry and lack of financial means. Mechnikov's ideas of controlling agricultural pests biologically found wide application only in the Soviet years. Today, not only micro-organisms (fungi) but other insects are used for this purpose, for instance, ladybirds and ichneumon-flies, which devour injurious insects or lay eggs in their larvae. However variegated and ingenious modern methods may be, it should be remembered that they are all based on Mechnikov's principle of utilizing inter-species struggle for the benefit of man.

* * *

This idea stimulated Mechnikov to study microbial antagonisms. The relations among different species of micro-organisms are highly varied. Some live in symbiosis, coexistence increasing their beneficial or harmful influence; other species inhibit one another's development, due to differences in their metabolic processes and in the resulting products. This is microbial antagonism. For instance, lactic acid bacteria living in the large intestine are antagonistic to pyogenic microbes; their metabolic products (in particular, lactic acid) exert an unfavourable influence on pus-forming bacteria, causing their death. The principle of inter-species struggle in microbes underlies the modern teaching of antibiotics, a major achievement of medicine of the last few decades. The use of such drugs as penicillin, streptomycin, and similar extremely potent drugs at the disposal of modern medicine, is also based on the principle of microbial antagonism.

* * *

The research of Pasteur and his assistants laid the foundation of a new science—bacteriology—and provided a potent stimulus to the practical fight against infectious diseases in animals and man through preventive and therapeutic vaccinations. Mechnikov admired this manifestation of progress in medicine. He often said and wrote that the work of Pasteur ushered in a new era in the life of humanity and constituted, along with Darwin's work on evolution, the summit of biological thought in the nineteenth century.

Having become aware of microbial antagonisms, Mechnikov bent all his energies towards combating infectious diseases.

At the end of 1883, he returned to Odessa, this time not as a professor but as a private citizen. He plunged into research work, and some of his major achievements, including observations on pathologic conditions in Daphnia and study of phagocytosis in tadpoles, belong to that period. His *magnum opus, The Embriological Study of the Medusae,* was also completed at that time. Nevertheless, his interest in the control of injurious insects did not abate and Mechnikov strengthened his ties with the Commission for Controlling Agricultural Pests. He waged a vigorous fight in behalf of his theory of phagocytosis. He read papers frequently at the Physicians' Society in Odessa and Kiev, at the Commission for Controlling Agricultural Pests, at congresses of agriculturists, delivered public lectures and held scientific consultations. He made frequent trips abroad, visiting Messina, Tangier, and Spain, where he studied intracellular digestion in marine animals. In 1883, his services to zoology received somewhat belated recognition, and he was elected corresponding member of the Russian Academy of Sciences. This served to console him somewhat for the hostile reception accorded to his theory of phagocytosis by the medical world.

In 1886, Mechnikov became the director of an institution which was a scientific centre, at the same time serving an intensely practical purpose—a Bacteriological Station, Russia's first and the world's second. The main task of the station was the preparation and use of preventive vaccines and sera for various diseases of man and agricultural animals, such as rabies, anthrax, foot-and-mouth disease, glanders and others, which caused great damage, to animal husbandry in the south of Russia, and in other parts of the country, as well as abroad.

Nikolai Gamaleya

Nikolai Gamaleya, later an outstanding Soviet bacteriologist but then a young physician, played a leading part in the founding of the Odessa Station and in its practical work.

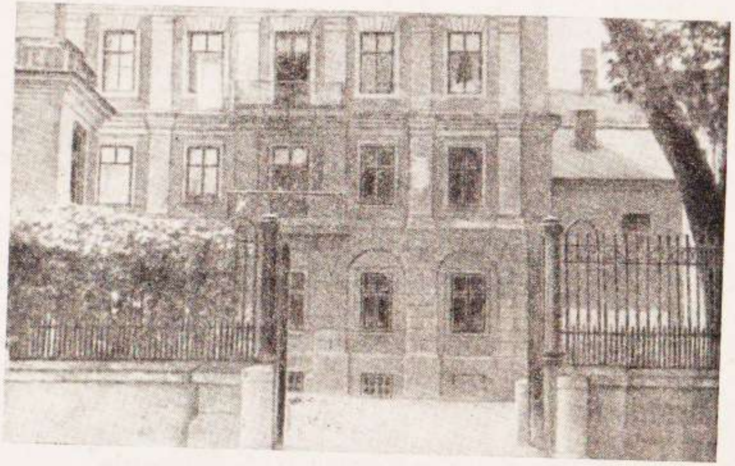
The opening of the Bacteriological Station in Odessa was intimately connected with the matter of anti-rabies vaccinations whose fame had spread all over the world. The Odessa Town Council decided to organize a bacteriological laboratory for diagnostic purposes, assigning a small sum of money for this. Simultaneously an anonymous benefactor (in reality, M. Stroyesko) donated 1,000 rubles to the Physicians' Society of Odessa to send a physician to Pasteur in order to study the methods of anti-rabies vaccinations. This physician was then to return to Odessa and put his experience into practice. The Physicians' Society sent N. Gamaleya to Paris. He stayed there several months, mastered the methods and returned with the material necessary for preparing vaccines supplied by Pasteur. On June 11, 1886, the Bacteriological Pasteur Station in Odessa began functioning. Its scientific staff was small, consisting of Mechnikov as director, Gamaleya as deputy director, young Dr. Bardakh as assistant director, and A. Ryabkov as laboratory assistant. Mechnikov's wife, Olga, and Gamaleya's wife made themselves useful in the laboratory. It was at the Odessa Station that D. Zabolotny, a young student who was expelled from the university for participating in a revolutionary students' meeting and who subsequently became a leading Russian microbiologist and epidemiologist, began his scientific career, studying the micro-organisms of snow and estuary water under Mechnikov's aegis. He identified a new species of phosphorescent infusoria and studied the cholera bacteria.

The station's premises consisted of five small rooms on the ground floor of a modest house in Gulevaya (now Lev Tolstoi) Street; Mechnikov lived with his wife in the flat on the first floor. The laboratory equipment was extremely inadequate lacking even a thermostat room, indispensable in any institution of this type.

In spite of the poor facilities, the enormous energy of its personnel enabled the station to accomplish much that

Yakov Bardakh

7—1760



Mechnikov's home in Odessa

was useful. In addition to giving vaccinations, the scientists at the station studied immunity to rabies and were able to determine the conditions under which vaccination proved most effective. Most of the credit for this work is due to Gamaleya.

In addition to rabies, the station staff studied other problems, such as methods of combating cattle-plague and cholera (an epidemic of cholera was expected in Odessa), means of diagnosing sputum for tuberculosis, and preparation of a vaccine against anthrax. In this connection, it should be mentioned that Gamaleya hit upon the brilliant idea of using killed bacilli in preventive anti-cholera vaccinations (later called chemical vaccine)—a method which subsequently found wide practical application.

Since one of the station's duties was to help agriculturists in combating pests, the biological methods proposed by Mechnikov in 1878-79 were studied and further elaborated. On January 20, 1888, at a session of the South Russian Society of Agriculturists, Mechnikov proposed to

fight susliks, which caused immense damage to agriculture, by infecting these animals with the bacilli of chicken-cholera.

Another aspect of the station's activities was educational work. It held courses for doctors, veterinary surgeons and other specialists in agriculture, arranged conferences and issued vaccine preparations.

One would expect the station to prosper and expand its work. Actually, however, it functioned under very unfavourable conditions, time and again encountering various, and often quite unexpected, obstacles.

The most inveterate opponents of the station and Mechnikov's sworn enemies were, surprisingly enough, certain physicians whose very profession presupposed that they should sympathize with him, rendering him every possible aid. But they were business-minded doctors, ardently pursuing their practice as a means of making a fortune; with his disinterested enthusiasm, Mechnikov appeared to menace their incomes. They declared war upon the station and Mechnikov personally; they carried on both open attacks during the sessions of the Physicians' Society and covert actions. Mechnikov's eyes were wide open to the machinations of his "honourable colleagues"; he saw perfectly well whence the storm-clouds came which were gathering over the station. This is what he writes in his *Reminiscences*: "It seemed things would go well. The new bacteriological institution set to work with a will but opposition soon raised its head.... The Physicians' Society began to deprecate everything that came from the new laboratory."

An ardent admirer of Pasteur and his school, Mechnikov attached a great deal of importance to micro-organisms, the agents of infectious diseases. This truly scientific approach opened up a practical path to means of controlling infections. But it was precisely these views that aroused the scepticism of certain Odessa doctors who characterized Mechnikov's work as a "senseless chase after commas" (meaning vibrios), "bacteriological fanaticism," etc. But open animosity was the least of the evils that befell the new station, especially since an open struggle could be waged against it. Covert actions constituted a much greater evil. They were carried on for a long time and brought about grave consequences. Here is an example of what they were like.

A St. Petersburg newspaper printed a feuilleton, doubtlessly inspired by an Odessa physician, which stated that the chicken-cholera bacilli which Mechnikov bred for inoculating susliks could transform themselves into the vibrios of Asiatic cholera; it further stated that his work constituted a grave danger to the population since an epidemic of the disease might break out. This article, written by an ignorant scribe, was sufficient for the Mayor of Odessa to order Mechnikov to stop his scientific experiments which were "endangering the population." Mechnikov wrote to Pasteur who answered: "There is no danger in trying to destroy some rodent or other in field conditions by employing chicken-cholera.... Many are the legends, my dear Mechnikov, which have been spread about microbiology since the new science has started developing in all directions.... The word 'cholera,' with its associations, is to blame; this is quite understandable but it is also devoid of any scientific justification whatsoever. There is no connection between the microbe of Asiatic cholera and that of chicken-cholera." (*Pages of Reminiscences*, 1946, p. 183.)

Mechnikov succeeded in having the senseless order recalled, but it cost him a great deal of mental and physical effort. He perceived that the prospect before him held little promise for work in his chosen sphere. The situation at the station, too, became complicated, because of disagreements among some of the personnel. Finally, something happened which brought everything to a head.

This something was the notorious "Pankeyev affair." An epizootic of anthrax broke out in the south of Russia

in 1887. Thousands of sheep perished, the losses running into millions of rubles. The flock belonging to Pankeyev, a local magnate, was also affected. He requested the station to vaccinate his sheep against anthrax. Four thousand head were vaccinated but the next day, three thousand died of anthrax. Whether they were already affected at the moment of vaccination or whether it was an act of revenge, remained an unsolved mystery. The yellow press, and Right-wing newspapers in particular, raised a hue and cry, hinting at intentional sabotage on the part of "red" laboratory workers, demanding that they be arrested and the institution closed. The authorities suspended the activity of the station. At the time of the disaster, Mechnikov was on vacation in the country. He came post-haste to Odessa and tried to unravel this dark and sordid affair and to secure permission for the station to proceed with its work. He spent much time and energy but he succeeded in reopening the station and continuing its useful work.

Actually this station is functioning today, for the Mechnikov Bacteriological Institute in Odessa is a reorganized and much enlarged version of the Bacteriological Station which he had set up in the eighties of the last century.

Apart from the unfortunate events going on at the station, Mechnikov had become convinced that, under the existing conditions, Russia was no place in which to carry on the work of combating infectious diseases. In his article "Why I Settled Abroad," Mechnikov says: "Upon finding myself in this situation, I felt that, as a theoretician, I would do best to leave, placing the laboratory in the hands of practical men. But since I wished with all my heart to go on with my research, I was obliged, at all costs, to find a peaceful shelter where I could devote myself to my studies." (*Ibid.*, 1946, p. 85.)

Mechnikov was aware that it was no chance mishap that the Odessa Bacteriological Station found itself in such narrow straits. The causes were deeper and more general. The ignorant but "ever-vigilant" powers that be, the narrow-minded and envious "pillars of society" (including influential scientific and particularly medical leaders), and last but not least, the political situation which curbed all independent scientific thought.

He realized the utter impossibility of devoting himself under the conditions existing in Russia at that time, to the realization of his dream—work in the field of theoretical science. He wrote: "The obstacles arising above, below and on all sides have placed this dream beyond realization." This by no means implies that he thought Russian scientists incapable of carrying on fruitful scientific work. On the contrary, he held them in high esteem, then and later entertaining a strong belief in the progress of Russian science. In the article mentioned above, he wrote: "One might think that the time has not yet arrived when science in Russia can be of use. I do not agree. On the contrary, I think that scientific work is necessary for Russia; it is my sincerest wish that conditions for such work become more favourable in the future than they were at the time I wrote about in the preceding pages." (*Ibid.*, p. 86.)

Despite his sanguine hopes for the future of science in Russia, Mechnikov could not have imagined the unprecedented scope of scientific research, including the fields of biology and medicine, attained in the Soviet Union. Numerous research and educational institutions named after Mechnikov, thousands of young scientists graduating every year from higher educational institutions and following in his footsteps—was it possible for him to conceive of this in the late eighties, as he was taking leave of his last and quite modest scientific venture in Russia—the Odessa Bacteriological Station?

In 1887, Mechnikov decided to go abroad. At first, he thought of settling in Germany, and accompanied by his wife, he visited laboratories in Wiesbaden, Munich, Strassburg, Frankfort and Breslau. The reserved and, at times,

openly hostile reception accorded him, prompted the great scientist to look for work and a home elsewhere. In the autumn of that year, he came to Paris to meet Pasteur and his co-workers. It was here that he spent the last 28 years of his life, working in close contact with the pupils and followers of the illustrious Frenchman. Although Pasteur and Mechnikov knew each other well and had maintained a lively correspondence, they had never met. Here is how Mechnikov described their first meeting: "On arriving at the laboratory for preventive anti-rabies vaccination, I saw an old man wearing a black skull-cap covering his close-cropped greying head, short of stature and partially paralyzed, with penetrating grey eyes, a grey moustache and a beard. His unhealthy, pale complexion and tired appearance told me that the man before me had not long to live—perhaps a few years, perhaps only a few months." (Mechnikov's sad prophecy was soon to come true—Pasteur died a few years later.)

"Pasteur received me very cordially and at once began to discuss the topic closest to my heart—the problem of the body's fight against microbes. He said: 'I placed myself at once on your side; I have been struck by the struggle between the diverse micro-organisms which I have observed. I believe you are on the right road.'"

At that time, a new and important centre of medicine and biology was being born in Paris. Pasteur was organizing his famous institute. Encouraged by the warm reception given him, and hearing about the vast building under construction, Mechnikov asked Pasteur if he would allow him to have a place to work in the institute. Pasteur welcomed the suggestion at once and offered Mechnikov a laboratory as well as the post of its chief, instead of merely a "place" with the role of "independent research worker" for which he had asked. It was but natural that Pasteur would make good use of this opportunity to include a world-famous scientist in his staff. They came to an agreement, and on October 15, 1888, Mechnikov settled in Paris.

At first, Pasteur put a room in his own laboratory at Mechnikov's disposal, but when the new building was completed, Mechnikov was given an excellent lay-out for his laboratory of which he was chief.

It would, however, be incorrect to assume that Mechnikov found conditions at the Pasteur Institute especially suited for work. In his article "The Pasteur Institute Becomes of Age" which appeared in the *Russkoye Slovo* (*Russian Word*) newspaper on November 21, 1909, Mechnikov presents a lively description of the poverty reigning there during the first seven years of its existence and of heroic attempts Pasteur and his assistants made in order to remedy this state of affairs. The institute was so badly off that when two horses were needed to prepare sera against tetanus and cholera, Émile Roux, one of the Institute's leaders, advanced the necessary sum from his own meagre funds. With devastating sarcasm revealing his social sympathies, Mechnikov described the attitude of the "money-bags," Rothschild and Hirsch, towards Pasteur's request for aid for his beloved creation.

The institute was saved from ruin and finally achieved some degree of material security due to the success of the anti-diphtheria serum and the considerable sum of money advanced by private benefactors. Incidentally, Mechnikov also described this with a great deal of humour and keen insight.

* * *

Mechnikov now entered upon a new stage in his life and career, which proved to be the last. During this period, Mechnikov resided abroad permanently but maintained a close contact with his native country which he visited several times.

How should we regard his decision to leave Russia for good? Was it, perchance, dictated by egoism and lack of courage? Perhaps he ought to have remained in his own country and continued his work at all costs? These questions troubled the minds of his contemporaries throughout all the years Mechnikov spent abroad; even today, these questions should be considered, if we are to delineate clearly the character of a great Russian scientist.

In answering these questions, we should bear in mind that conditions in tsarist Russia prevented Mechnikov from continuing his scientific work, that he was actually driven away, first from the university and then from the Bacteriological Station, because of his being considered a "red" professor and a "trouble-maker." The entire situation was such as to make adequate scientific research impossible. Mechnikov was unable to choose his assistants, because those whom he desired to have were (or could be) considered unacceptable for political or national reasons. A professor who was known to associate with student youth, was committing a mortal sin and a sharp eye had to be kept on him. University professors often did not rise above mediocrity but were politically reliable.

Mechnikov would not tolerate anything which fell short of his high ideals; he was unable to work in tsarist Russia and therefore emigrated. However, he did not lose his ties with his native country; he did not become a foreigner. If anything, his ties with Russia became stronger and more intimate with the passage of time.

In Russia, he had fast friends who were close to him ideologically and had common scientific interests; among these were I. Sechenov, A. Kovalevsky, N. Umov and S. Vinogradsky, with whom he never lost touch. In his Paris laboratory he welcomed scientists who came from Russia, especially those who were unable to work in their native land. As he said in 1913: "My laboratory is open to all Russian scientists who desire to work and who can work; in it, they can find a home." A whole galaxy of Russian scientists availed themselves of his invitation. Among those who worked in Mechnikov's laboratory were Zabolotny, Bezredka, Tarasevich, Volman, Savchenko, Tsiklinskaya, N. Chistovich and F. Chistovich, Khavkin and others—the pride of world, as well as Russian, science, some of whom were the founders of new branches of medicine, such as microbiology, epidemiology and immunology. In addition, Mechnikov maintained contact with the Russian colony in Paris, which consisted chiefly of revolutionaries who had fled from Russia for political reasons.

Progressive Russian men and women have never regarded Mechnikov as an *émigré*, who abandoned his country willingly. They always felt sympathy with the scientist whom circumstances compelled to live abroad. In this respect, the words of V. Zelensky, a well-known zoologist who was a schoolfellow and close associate of Mechnikov's, are of great significance. This is what he wrote in his article dedicated to the memory of Mechnikov: "Regrets are often expressed that Ilya Ilyich left Russia at the zenith of his scientific activity and settled in Paris where he spent the greater part of his active life. These regrets may be well founded and are shared by those to whom the progress of Russian science is a matter of great concern.

"If, however, we take into consideration the fact that a very large number of Russians worked in Mechnikov's laboratory in Paris under his guidance, and under such favourable conditions as were not to be found in Russia, we may be consoled that Ilya Ilyich's work, done outside of Russia, has proved to be highly beneficial to science inside Russia."

Although living abroad, Mechnikov did not betray the interests of his country, preserving his ties with it to the end of his days; in a word, he did not cease being a Russian. His answer, "I was and am a Russian," which he sent to the Nobel Prize Committee in 1908 when he was asked about his nationality, is very explicit and full of national pride. Russia has always regarded Mechnikov as the flesh of her flesh, has been proud of him and honoured him as one of her sons. As we shall see

later, attempts were made repeatedly to recall him to Russia; but the political atmosphere was too strained, and Mechnikov, although not without much hesitation and doubt, invariably refused.

FIGHT FOR THE PHAGOCYTIC THEORY OF IMMUNITY

The period we have just described was one of the most eventful in Mechnikov's exceedingly rich and fruitful scientific career. We may designate this period as "the period of the fight in behalf of the theory of cellular (phagocytic) immunity."

Fully conscious of the exceptional—not purely theoretical but also practical—significance of his theory of phagocytic immunity, Mechnikov took his time in selecting his factual data and in giving a more precise form to his ideas before he decided to publish his new theory. He exercised a restraint and caution which was quite out of keeping with his volatile nature. There is evidence that, as early as the end of the seventies, Mechnikov had mentioned the enormous biological import of intracellular digestion in his lectures at the university. The first public presentation of the phagocytic theory of immunity was made at a much later date—in August 1883, in his speech, "The Curative Forces of the Organism," delivered in the capacity of chairman of the Seventh All-Russia Congress of Naturalists and Physicians in Odessa. In his speech, he outlined the fundamental premises of the theory of phagocytosis. Eight months had elapsed between his discovery made at Messina and the day he made his new theory public; the intervening time had been spent in verifying his experiments and in working out their theoretical basis. Mechnikov had been in no hurry to publish his views, but once they were published, he defended them with extraordinary consistency, tirelessly and unflaggingly, with every available means: he published his experiments, he read papers at scientific conferences, he made reports at international congresses. Mechnikov had prepared himself for the fight; he was not disappointed—there were fights aplenty. At a congress of the British Medical Association in 1896, Lord Lister, the great British surgeon, said, when the fight was nearing its end, that if ever there was a romantic chapter in pathology, it certainly was the theory of immunity. Mechnikov was not alone in this struggle. He enjoyed the support of his numerous pupils and scientists working in other institutions; he had the moral support of Pasteur and Lord Lister, and the experimental results obtained by some other great scientists, for instance, Émile Roux, were especially helpful to him. Mechnikov was the only acknowledged leader in the campaign in behalf of the theory of phagocytosis.

The world of medical science accepted the biological theory of inflammation without any show of enthusiasm. Its significance was appreciated—and even that not immediately—by such eminent scientists as Virchow, Ribbert, and the far-sighted Pasteur. But the theory of cellular immunity, upsetting as it did the accepted notion of the cause and development of infectious diseases, aroused hostility in the high priests of official medical science, particularly in Germany. They were indignant that a Russian zoologist, far removed from medicine, dared to encroach on their preserves, questioned their age-hallowed canons, ventured to express new and unexpected views, made suggestions. There was reason enough for the entire Areopagus of medicine, and even for those in the ranks of the medical fraternity, to cry "murder." It was but natural that Petri, a pupil of Koch's, should describe Mechnikov's theory as an "Oriental fairy-tale."

The pathologists were the first to declare war on Mechnikov. Baumgarten, a German pathologist, one of the pillars of the old medical theory, stated in the

press that "Mechnikov's observations are not only insufficiently grounded but even contradict logic and truth." Elsewhere, he wrote that "Mechnikov's explanation of the activity of leucocytes is proof of his fertile imagination rather than the result of objective observation done by a research worker." Other scientists, including Ziegler and Weigert, also denounced Mechnikov's theory. Even Virchow—who had been in Messina in the spring of 1883, seen Mechnikov's preparations and could not deny the factual data bearing on phagocytosis—even he advised his "friend" to be careful about his conclusions which were at such crying variance with accepted opinion.

The essence of the pathologists' objections to Mechnikov's theory lay principally in their denial of the existence of a struggle between bacteria and leucocytes, the phagocytes of higher animals. Some were even of the opinion that bacteria existed in a state of symbiosis with leucocytes, utilizing them as a means of locomotion; others, and these were in the majority, maintained that leucocytes devoured only dead bacteria, acting as scavengers, as it were, and could, naturally, play no important part in the body's fight against infection. The most important argument advanced was that, in precisely those cases where the blood and tissues were filled with microbes, phagocytes were not to be seen—they "had deserted the battle-field."

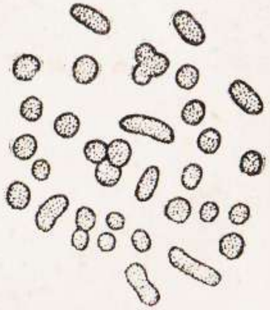
By means of experiments, Mechnikov defeated the arguments of his opponents and proved his point by showing that phagocytes devoured not *dead* but *live* microbes—this could be observed under the microscope, for instance, when leucocytes engulfed mobile bacteria, such as *Bacillus pyocyaneus*; the bacteria could be seen moving about for some time in the protoplasm of the phagocyte even after they were ingested. Czaplewsky, a pupil of Baumgarten's, published a treatise in which he explained the natural immunity of pigeons to anthrax by postulating that the tissue fluids of the host destroy the bacilli. When facts compelled him to acknowledge the phenomenon of phagocytosis, he tried to relegate it to a place of secondary importance by insisting that phagocytes devoured only dead microbes and did not even try to destroy live ones. In reply to this, Mechnikov staged a very complex but highly convincing experiment. He introduced a culture of anthrax bacillus into the anterior chamber of a pigeon's eye and some time later, removed an aqueous fluid from the chamber containing a large number of leucocytes which had engulfed the bacteria. This liquid was placed in a culture medium and kept in a thermostat at 37°C., so that individual leucocytes could be observed all the time. Somewhat later, the leucocytes died, and a guinea-pig was inoculated with some bacteria thus freed. The animal died, revealing a typical picture of anthrax. The experiment proved that leucocytes engulf live bacteria which are then digested by the phagocytes' protoplasm.

Furthermore, Baumgarten denied the existence of any connection between immunity to a given disease and phagocytosis. Baumgarten's pupils tried to prove that the frog's immunity to anthrax was not the result of phagocytic activity, but was due to the destruction of bacteria by fluids within the organism. This is how Mechnikov disproved this assertion. Spores of the anthrax bacillus, protected by capsules (made of filter paper or bulrush pith) from attack by phagocytes, were introduced subcutaneously into a frog. The anthrax bacilli were protected inasmuch as the phagocytes could not penetrate through the capsule walls. But the bacilli were left exposed to the action of body fluids. The spores suffered in no way; on the contrary, protected from phagocytes, they germinated and gave rise to flourishing colonies in what proved to be an excellent culture medium. His experiments convincingly demonstrated the defensive role played by the phagocytes.

But Mechnikov's opponents were ready with a new argument. They drew attention to the fact that phagocytes

were absent from the blood and tissues when an infection took a very severe course. Mechnikov's biological experiments with the germinating spores of a mould fungus in the Daphnia were able to furnish a fairly tenable explanation. When the spores were introduced in exceptionally large amounts, the phagocytes all but disappeared. They died since they were unable to withstand the fulminating infection. The absence of leucocytes in the blood and tissues, teeming with microbes, proved not the *passivity* of the phagocytes, but their *death* in an unequal struggle against a stronger enemy.

Thus Mechnikov was able to refute the pathologists' objections. Proving his point to the bacteriologists (Mechnikov was a bacteriologist himself) presented a more difficult task.



Cholera vibrios destroyed in the fluid of the peritoneal cavity of an immunized guinea-pig (the Pfeiffer phenomenon)

In 1884, V. Groman, a Russian scientist, and later Fodor and Nuttall, proved that bacteria were destroyed by defibrinated blood (blood deprived not only of red and white corpuscles but of the clotting matter, fibrin, as well). Flügge, who wished to reconcile the theory of phagocytosis with this discovery, postulated that serum contained bactericidal substances and that the leucocytes then devoured the bacteria already killed by these substances. More and more factual data were being supplied by leading progressive bacteriologists. Behring, for instance, asserted that natural and acquired immunity was connected with the properties of blood plasma and lymph. Many scientists, including Mechnikov, were greatly impressed by the experiments of Isayev and Pfeiffer who demonstrated that, when virulent cholera vibrios were inoculated into the peritoneal cavity of a guinea-pig immune to them, the vibrios were destroyed without the participation of phagocytes All these data served to lay the foundation of a new, humoral theory of immunity, attributing particular importance to the body's tissue fluids. This placed the idea of phagocytic, cellular, immunity in the background.

At the International Hygiene Congress in Berlin in 1890, Koch stated that it was his opinion that the phagocytic should give way to the humoral theory. Fraenkel, an eminent German scientist, wrote in his textbook: "Science has discovered the means by which the body protects itself against its most dangerous enemies—means having nothing in common with phagocytosis and acting quite independently of the latter."

The theory of phagocytosis seemed to have been struck at the roots and finally condemned by the leading lights of science, but Mechnikov would not give in and continued to fight for it with all his wonted vigour and energy. He carefully examined the Isayev-Pfeiffer phenomenon and proved that phagocytes participated in this instance as well. He showed that leucocytes were destroyed by a bacterial culture introduced into the peritoneal cavity (he called this phagolysis), but the digestive enzymes they contained were released into the surrounding medium (the fluid in the cavity), thus enabling it—the peritoneal cavity fluid—to dissolve bacteria. When the experiment was staged differently, i.e., when a mass of leucocytes was attracted to the peritoneal cavity by a previous injection of broth, the course of the defensive reaction was altered, the bacteria destroyed by the phagocytes and not dissolved in the fluid medium.

Some data, however, obtained by Mechnikov's own assistants and not by his opponents, did not conform with the original scheme of the theory of cellular immunity. Phagocytes were found to contain within themselves a substance (which some called alexin and others, complement) which, escaping from destroyed leucocytes into a

liquid medium (primarily blood and lymph), possessed bactericidal action. On the other hand, blood was found to contain substances facilitating the action of leucocytes: these substances either agglutinated bacteria (agglutinin) or increased the phagocytic efficiency of the leucocytes by attracting them to bacteria or changing their chemotaxis from negative (often the case) to decidedly positive.

V. Isayev, a talented Russian doctor working in Mechnikov's laboratory at the Pasteur Institute, established that tissue fluid, altered by pneumococcus toxin, stimulated the activity of phagocytes by enhancing their ability to engulf and digest bacteria. This substance was later studied in detail by Wright and named opsonin.

Gradually facts accumulated, showing that leucocytes were not mere phagocytes engulfing and digesting harmful and foreign particles penetrating the body. It was discovered that they elaborated and released into the blood or lymph various substances—antitoxins—capable of agglutinating the toxic products of microbial activity or otherwise rendering them harmless.

Still later, it was discovered that phagocytes secreted certain other substances—enzymes—stimulating the activity of tissue fluids, facilitating the healing of wounds, and exercising a tonic effect on the whole body. The original idea of the role of the leucocytes had to be materially revised and expanded.

For all his enthusiasm in matters of science, Mechnikov was not a narrow-minded dogmatist trying to fit his facts into the Procrustean bed of preconceived ideas. On the contrary, his was the objective mind of a great scientist, capable of openly acknowledging his mistakes and correcting his conceptions, even if long-entertained, when facts made this imperative. So, while attributing a role of paramount importance to phagocytes in the struggle against infection, he wrote: "But this by no means implies that there will be no more discoveries relating to other influences assisting phagocytes in this struggle." And indeed, we now know that chemical substances, elaborated by the blood and other tissues, play a very important part in the system of the body's defensive measures. Thus, out of frank exchange of opinions, out of the beneficial crossfire of lively scientific discussion, there arose a modified, more precise phagocytic theory of immunity. Its significance did not diminish with the passage of time, and beginning with 1891, science began to show a favourable attitude towards the theory. Outstanding scientists, —Roux, Bouchard and Flügge—took up arms in its defence; Behring changed his negative attitude, and even Buchner, a rabid enemy of Mechnikov's theory, tried to reconcile the phagocytic with the humoral theory. Gradually Mechnikov's theory won a place of honour in the treasury of pathology's fundamental ideas. This process may be illustrated by the change of attitude towards the theory, observable at successive international medical (usually—hygiene) congresses. At the Vienna Congress in 1887, the theory was attacked by the overwhelming majority of speakers. At the congress held in London in 1891, Mechnikov gained the support of Lord Lister, the great surgeon and founder of the doctrine of antisepsis. As chairman of the Bacteriological Section first founded at that congress, Lister allowed Mechnikov to speak for fifty minutes although the time limit was fifteen. Lister himself, in his concluding remarks, expressed a favourable opinion. He stated his point of view even more forcibly in a speech on "The Art of Healing and Science," made in 1896. In discussing the reasons why a septic centre is not formed and why septicaemia does not occur when wounds are treated with water dressings, he attributed it to the action of phagocytes. He added that phagocytosis undoubtedly played a certain role in the fight against microbes in the air and that the investigation into phagocytic reaction had contributed largely to the theory of antisepsis in surgery. (*Immunity in Infectious Diseases*, 1953, pp. 481-82.) At the congress which convened in

Budapest in 1894, Buchner stated that it should be admitted that phagocytes played a prominent part in the humoral theory, that alexins were produced by phagocytes, but that the latter were capable of digesting only dead bacteria. But at the International Congress in Paris in 1900, this same Buchner admitted the decisive part played by phagocytes during that phase of the immunity reaction when the activity of their products—the alexins —was not strong enough for one reason or another. The majority of pathologists, bacteriologists and clinical physicians present at the congress accepted the theory of phagocytosis. This, in turn, influenced the authors of popular textbooks. Whereas in the first edition of his textbook of bacteriology, Günther said: "The phagocytic theory has been proved untenable," in the fifth edition of the book (1898), he devoted considerable space to the exposition of the theory, attempting to reconcile it with the humoral theory of immunity.

In his turn, Mechnikov changed his opinion that intracellular digestion was the only defensive mechanism of phagocytes. He acknowledged the role played by substances secreted by cells (alexins, or fixators), as well as that played by chemical substances (antibodies and antitoxins) which agglutinate and render harmless those foreign bodies formed in the organism as a result of bacterial activity or those which are introduced from without. But while acknowledging all this, Mechnikov remained true to his theory of phagocytosis, since he attributed the production of defensive substances to phagocytes, both mobile and non-mobile blood cells—macrophages—occurring in large quantities in almost all organs. Subsequent research carried out by other scientists substantiated the latter viewpoint, and today the accepted idea is that the macrophage endothelial system of the body produces antibodies.

In 1908, Mechnikov's works on immunology received world recognition. He was awarded a Nobel Prize. In his speech in Stockholm in May of 1909 he said: "The complex

A group of participants in the Bacteriological Section of the Seventh International Hygiene Congress held in London in 1891. Sixth from the left in the middle row is Ilya Mechnikov; second and third from the left in the first row are Emile Roux and Lord Lister

of all the phenomena observed in the process of immunity can be reduced to a number of biological factors, such as the sensitivity of phagocytes, their active interference in places which are threatened with microbial attack, as well as to a number of physico-chemical causes which result in the destruction and digestion of agents of infection."

The prize was given both to Mechnikov and to Ehrlich, an outstanding protagonist of the humoral theory.

Twenty-five years were to pass in indefatigable struggle before the phagocytic theory of immunity overcame all obstacles, provided answers to all the questions and became one of the golden truths of science. That this was at all possible was due to the inexhaustible energy, experimental inventiveness, enthusiasm and unshakable confidence in the correctness of his views—qualities which

astonished Mechnikov's associates and contemporaries. His friend, Roux, wrote to him: "Your ardour kindles the indolent and inspires sceptics with confidence." And touching upon Mechnikov's speech at the London Congress, he said: "He spoke with such passion that everybody was aroused. I think that today the theory of phagocytosis made many friends for itself." Especially vivid is Roux's description of Mechnikov's appearance at the Budapest Congress in 1894, one of the most important: "I see you before me as you were in Budapest in 1894, arguing with your opponents; your face all aflame, your eyes sparkling, your hair dishevelled. You were like a genie of science; your words and your unassailable arguments evoked the applause of the audience."

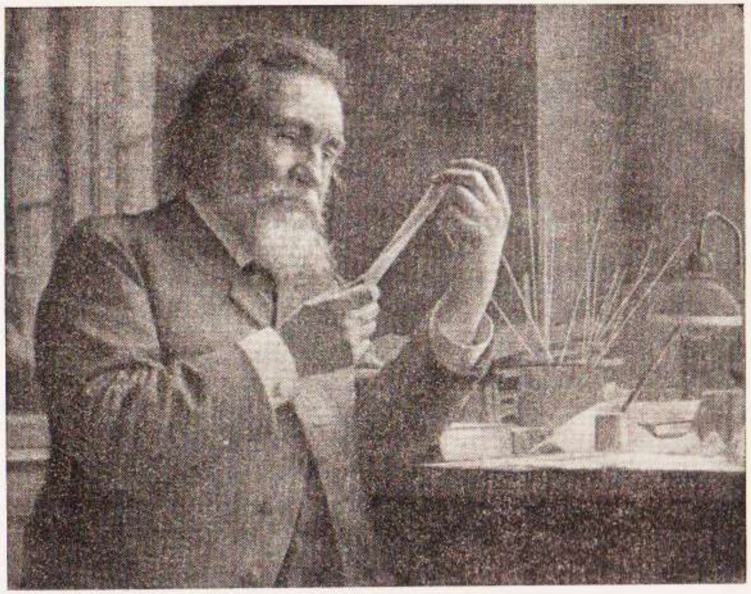
It was a victory but by no means an easy one!

In his autobiographical notes, written towards the end of his days, Mechnikov says: "The polemics about the phagocytes could have killed me or undermined my strength completely.... There were times (for instance, the attacks of Lubarsch in 1889 or of Pfeiffer in 1894) when I was on the point of committing suicide." Olga Mechnikova, too, speaks of the enormous effort the theory of phagocytosis cost her husband. "Only his intimate friends knew the amount of vital energy he spent in this struggle ... how many sleepless nights he passed because his brain was continually thinking up new experiments that would be convincing and definitive; what a sea of emotions, sad and joyous, he experienced!"

In withstanding the many tests it was put to, the theory of cellular immunity acquired a host of new and important proofs, became an integral part of the concept of the role played by chemical substances in the body's defences and of the significance of the state of the host for the development of immunity. Rejuvenated and invigorated, this theory became a fundamental doctrine of medicine and a cornerstone of a new science—immunology. As Roux wrote to Mechnikov: "Today, my dear friend, you may look upon this doctrine of phagocytosis with the quiet satisfaction of a father whose son has been successful in the world. But what anxiety and effort it has cost you! Its appearance provoked protests and resistance and, for twenty years, you have been fighting for it. One must have lived with you during that period of fight, to understand how much joy and suffering scientific research could cause a person enamoured of it. And just see the great results you have achieved, with very simple methods—the mark of genius!"

MECHNIKOV AT THE PASTEUR INSTITUTE. STUDY OF CELLULAR TOXINS. MICROBIOLOGICAL RESEARCH (1888-1916)

The last years of Mechnikov's life were not marked by any spectacular events. The atmosphere at the Pasteur Institute was extremely favourable. After a short period during which Mechnikov and his new colleagues were getting to know one another, and during which the latter might have eyed him with certain doubts, relations became amicable, even cordial, and Mechnikov found himself in a surrounding highly conducive to fruitful work. Pasteur and his closest associates and successors, Roux and Duclaux, thought highly of Mechnikov and considered him an excellent acquisition to their institute. In the letter we mentioned above, Roux wrote: "It is no wonder that Pasteur welcomed you with open arms: you brought him nothing more or less than a doctrine of immunity." It was quite natural for the sphere of Mechnikov's activities to expand at the institute. His laboratory became one of the most important and well staffed. This was due, in no small measure, to the love which both budding and mature Russian scientists cherished for Mechnikov. Among the vast numbers that flocked to his laboratory from all parts of the world, Russians were the most numerous. For them, Mechnikov represented the final authority and was an unsurpassed teacher. He proved to be a well-disposed and understanding friend; everyone was eager to come in contact with this wonderful man.



Ilya Mechnikov in the laboratory of the Pasteur Institute

Mechnikov played a conspicuous role in the life of the Pasteur Institute. In 1903, he was appointed its deputy director and occupied this post for many years. But apart from his official position, his talent, erudition, and unimpeachable human and scientific honesty stamped their mark on the general character of the institute and influenced the trend of its work. Mechnikov was very popular with French scientists, too. In 1909, when a delegate was to be sent to Cambridge for the celebrations of Darwin's hundredth birthday, he was chosen as a delegate, representative of the Pasteur Institute (and indeed of the whole of France) to that assembly of the world's scientists.

At last, his work won general recognition. Indifferent as he was to all show, a deluge of medals, orders and prizes descended on him. That the honours in themselves were not Mechnikov's objective can be seen from the friendly, if slightly ironical, account of the eagerness with which another great scientist—Pasteur—accepted such signs of official recognition: "After dinner, doubtlessly desiring to please my wife and me, he showed us a case containing the numerous orders which he had been awarded. In order to make a still deeper impression on us, he drew out an order, made of little roses and hung on a chain, and solemnly announced that it was a very high Brazilian order, granted only to two persons—to himself and to a Brazilian admiral. I could not help remarking that it was no great honour for Pasteur to be treated like an admiral, even a very deserving one." (*Pages of Reminiscences*, 1946, pp. 88-89.)

What Mechnikov did appreciate were prizes and honorary titles conferred by scientific bodies such as academies and universities, because he felt they constituted recognition of his services to science by unbiased, and at times even originally sceptical, colleagues. In his autobiography written in 1909 in connection with the award of his Nobel Prize, he mentioned some of the honours conferred upon him: he was a D. Sc. *honoris causa* of Cambridge University, a Foreign Member of the Royal Society of London, a member of the Academy of Medicine of Paris, a corresponding member of many academies of sciences; he also received numerous medals from scientific societies, including the Wilde Gold Medal (from the Literary and Philosophical Society, Manchester, 1901), the Copley Medal (from the Royal Society of London, 1906), the Albert Medal (from the Royal Society of Arts in London, 1916). In announcing this last award, *Nature**

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* July 6, 1916, p. 386.

wrote:"The Albert Medal of the Royal Society of Arts for the current year has been awarded to Prof. Elias Metchnikoff, For. Mem. R. S. ... The annual report of the council, published in the Journal of the Society for June 30, refers to the award as follows: 'The discoveries of Prof. Metchnikoff in regard to the nature of immunity to infective diseases have contributed, more than the work of any other living man, to the control of such diseases, and to the consequent improvement in the health of great European populations, and the safeguarding of those who have to face the dangers of bacterial infection, whether on the battle-field or as pioneers in tropical climates.'" And, finally, he received the highest scientific honour known in those days—the Nobel Prize.

Scientific institutions of his own country, even those which had caused him no little trouble in their time, also recognized Mechnikov's merits, although somewhat belatedly. In 1902, he was elected Honorary Academician to the Russian Academy of Sciences which had refused him the Baer Prize; in 1909, the Military Medical Academy (formerly Medico-Chirurgical) which had blackballed him in 1870, conferred on him the degree of D. M. *honoris causa* and elected him Honorary Academician. Consequently, there was every reason for Mechnikov to be satisfied, and the fifteen years beginning with the year when he turned fifty were the happiest in his life. The smooth course of his life was ruffled from time to time by petty everyday troubles, but the hypersensitivity which had brought him so much suffering in his youth gave place to composure and to an optimistic acceptance of life. His love of nature and keen interest in science and art gained in intensity as did his solicitude for those around him. In 1898, Mechnikov bought a small villa at Sèvres, about half an hour's train ride from Paris. In 1903, he settled there permanently, since he liked the country and considered daily walks to and from the railway station very wholesome. This was at a time when Mechnikov wanted to test on himself the correctness of his theory of orthobiosis of which more will be said later. He began living in accordance with a fixed schedule; work alternated with rest, and he went on a diet of boiled fruit, vegetables and sour milk. On coming home at seven in the evening, he put his work aside and spent his evenings reading, playing music and conversing with his friends. Life flowed on pleasantly and harmoniously. Those were indeed the happiest years of his life.

* * *

What were the activities in which he was engaged during those happy and fruitful years? First and most important, he fought for his theory of phagocytosis. As we have seen, in the first half of this period (1888-1900), the struggle was at its hottest, filled with many dramatic incidents. His two chief works, *Comparative Pathology of Inflammation* (1892) and *Immunity in Infectious Diseases* (1901), giving a distinct and consistent exposition of his views, were largely the outcome of his struggle.

Beginning with the last years of the previous century, Mechnikov devoted much time and energy to the experimental and theoretical investigation of old age. In addition to a number of smaller monographs on the results of his laboratory experiments, Mechnikov wrote three extensive works on this subject—*The Nature of Man* (1903), *Studies in Optimism* (1907), and *Forty Years' Search for a Rational Outlook* (1913). But if we wish to follow the development of the one scientific idea that dominated all his life and work, we should turn our attention to his research concerning the organism's reaction to the influence of foreign bodies.

We know that phagocytes, alive or dead, secrete substances (Mechnikov called them *cytases*) which possess bactericidal properties. It was further found that not only microbes but their poisonous vital products—toxins—can also be rendered harmless within the organism, because antitoxins appear in the blood of the infected subject.

Antitoxins are substances capable of agglutinating and rendering harmless poisons—not only those of microbial origin. Mechnikov succeded in establishing that these substances are also produced by phagocytes. A. Bezredka, a well-known bacteriologist and pupil of Mechnikov's, proved that if a minute dose of trichlorarsenic, a toxic coloured substance, is introduced into the body, its granules may be found within the phagocytes; the organism, far from sustaining any injury from the poison, will thus acquire resistance to much larger doses of it. This is where the defensive substances produced by phagocytes come into play. When phagocytes are prevented from attacking toxins directly (for example, when a non-lethal dose of trichlorarsenic is introduced in isolating bulrush or elder capsules), or when the reaction is blocked by a harmless substance, say, carmine, the body, deprived of its chief means of defence, will either die or suffer greatly. In the period under consideration Mechnikov was occupied by an all-around study of antitoxins. He established that they were contained in the tissue fluids (mainly in blood) rich in phagocytes, and also in what he called "phagocytic organs"—the spleen, lymphatic nodes and the blood vessels of the liver. Macrophages, or large non-mobile cells, can render toxins harmless. Further research revealed an even more significant role played by macrophages in the life of living organisms. Thus Mechnikov passed from the particular problems of the body's defences against microbes and their toxins to a more general one concerning the body's reaction to foreign invasion. He approached this phenomenon from the biologist's point of view, regarding it as the ability of organisms to evolve defensive reactions in response to foreign protein substances. In this way, he laid a basis for the theory concerning foreign protein substances—antigens—and the substances which neutralize them—antibodies. Antibodies are elaborated mainly (if not exclusively) by macrophages within the macrophage-endothelial system mentioned before. Mechnikov, as a biologist, was interested in the immuno-biological reaction not only to microbes or their toxins, but to any foreign protein introduced into the organism. He studied the body's reaction to the introduction of foreign blood corpuscles. He showed that here intracellular digestion by phagocytes, which enveloped foreign blood cells, proceeded concomitant with their destruction by haemolysins, special substances produced by phagocytes, particularly macrophages. The presence of these substances makes the haemolysis of foreign blood elements possible. If an animal, in whose body haemolysis of foreign blood cells has taken place, is given a new dose of the same blood (for instance, the blood of a bird containing nucleated red corpuscles is injected into a rabbit), haemolysis will proceed at a faster rate and more completely than it did the first time. This means that it is a typical defensive immuno-biological reaction involving the production of specific defensive substances against foreign blood elements. In the course of his experiments, Mechnikov observed the same defensive reaction, not only in the case of foreign blood, but with extracts from different organs and tissues, such as testicles, kidneys, liver, ciliated epithelium, etc. The blood then reveals the presence of specific defensive substances which he called cytotoxins or cellular poisons. These defensive substances are produced in such large quantities that they act even when introduced into the blood of other animals. This phenomenon is relatively less pronounced when the organs of animals belonging to the same species (homocytotoxins) are used, and more pronounced when the organs of animals belonging to other species (heterocytotoxins) are used. A vivid illustration of the latter was supplied by the experiments of Bordet, an outstanding Belgian bacteriologist and a pupil of Mechnikov's. He showed that if blood elements of a rabbit are repeatedly injected into a guinea-pig, its serum acquires the ability to dissolve the foreign blood cells as the serum becomes rich in heterohaemolysins. Mechnikov's investigations in this sphere possess great theoretical value, since he proved that each species, each individual, and each organ possesses its own specific immunity which determines the complex relations between an organism and its environment. Mechnikov regarded these complex reactions of immunity in the broadest sense of the term as an adaptation of organisms to environmental influences. He showed that these reactions can be intensified or weakened, depending on the nature of external influences. In this way, Mechnikov explained the mechanism of the adaptive reaction of the organism to external influences, a manifestation of which is the destruction of harmful substances penetrating into the body and the production of subsequent immunity. He explained all this on the basis of sensitivity of the protoplasm of living cells to irritation. Altogether, he attached a great deal of importance to this property whose manifestations he observed in other familiar functions of cells and entire organisms, such as the different forms of directed motions (photo-, geo-, chemotaxes, the movement of the processes of nerve cells towards the muscle fibre, etc.). He was apt to exaggerate somewhat the importance of this primitive sensitivity, attempting to explain in this way the complex reactions peculiar to the higher forms of reactive activity encountered in higher animals and the nervous activity of man, about which we shall have an occasion to write later on. What we want to emphasize here is that this generalization, one may say "biologization" of the notion of immunity, was highly characteristic of Mechnikov, a Darwinist and biologist with a limitless scope of interests.

* * *

The problems of the immuno-biological reactions of living organisms, of organ specificity and of cytotoxins, however, are not purely theoretical ones, but have a significant bearing on practical biology and medicine. One sphere in which the problem of individual specificity is of paramount importance is the practice of transplanting and grafting tissues and whole organs. Here science encounters manifold difficulties because of the incompatibility manifested even by homotransplants, i.e., tissues and organs taken from an animal of the same species. Frequently, the grafted tissue is dissolved a short time after transplantation. Today scientists are searching for ways and means of putting a stop to this reaction which prevents the transplant from becoming an integral part of the host organism.

There is another sphere of medicine in which Mechnikov thought the teaching of immuno-biological reactions could be used with advantage. Since cytotoxins exist, it is probable that the organism could elaborate its own antidotes, anticytotoxins. And indeed, he cited numerous data (beginning with Bordet's experiments with haemolysins), showing that phagocytes did produce anticytotoxins which were not specific for a given species. This might enable the production of anticytotoxins, prepared from animal tissues and organs and serving to defend those same parts of the human body. Mechnikov held that such anticytotoxins might be helpful in combating malignant growths. Cytotoxins could be utilized as such. Bearing in mind the premise that minute quantities of poison stimulate the activity of organs and tissues, Mechnikov expressed the view that small doses of cytotoxins, too, might exhibit this property and that an attempt should be made to use them for therapeutic purposes.

This clever idea of Mechnikov's was recently extensively elaborated by Academician A. Bogomolets and his assistants who were experimenting with an antireticular cytotoxic serum. They studied the effect of stimulating (minute) doses of a serum containing cytotoxins on the most important defensive phagocytic system of the body. (To obtain this serum, animals are usually injected with an extract from the spleen). At first, this method appeared to have a definitely favourable therapeutic effect, but

the hopes it aroused were not justified; the antireticular cytotoxic serum was *not* a cure-all, as some of its advocates had asserted. Yet there is reason to believe that minute doses of cytotoxins (especially those produced by the reticular-endothelial system) can stimulate the activity of the body or of some of its systems. The problem of the use of cytotoxins or, in a wider sense, of organotherapy, first raised by Mechnikov, has yet to be studied in all its implications.

* * *

The problem of cellular poisons and antidotes represented to Mechnikov another, somewhat unexpected, matter of interest. Since these poisons and antidotes figure so importantly in the life of the organism, Mechnikov thought that perhaps he could resort to them not only in cases of sickness, but also for the purpose of combating the process of ageing. The work he did in the early eighties showed that phagocytes were the decisive factor in restoring the organism to normal, after various atrophic alterations in tissues, for instance, metamorphosis, had taken place. In his later work, Mechnikov explained that, among the widely different cells unified under this category, it was the macrophages which destroyed cells and animal cell residues; his final conclusion was that senile atrophy was the result of intensified activity on the part of the macrophages. This activity could be stimulated by weakening the organism's specialized elements. Such atrophy could, therefore, be combated either by inhibiting the macrophages or by strengthening the specific elements of the organism. Cytotoxins and anticytotoxins might be utilized for this purpose. If the attempts to make use of them in this connection were successful, man could then so influence the process of ageing as to retard it. In this way, from the problems of immunity, cellular poisons and antidotes, Mechnikov arrived at a problem of immense biological and philosophical significance—the problem of old age—to the study of which he devoted the last fifteen years of his life.

Before we consider his achievements in this all-important sphere of biology, we should touch upon the work in bacteriology which he completed during his years at the Pasteur Institute and which proved to be of extreme value to medicine.

* * *

Above all, mention should be made of the investigations on cholera which he conducted in 1893-96. His interest in cholera was by no means fortuitous; Mechnikov had long been interested in the problem of intestinal digestion in higher animals and man. Besides, at that time, endemic outbreaks of cholera were observed in France, Russia, and some other countries, but the causative agent of this disease was not yet definitely established. Mechnikov and his collaborators succeeded in establishing that the cholera vibrio was the pathogenic agent. To prove this, he and six of his colleagues swallowed weakened cholera vibrios; the results were strikingly convincing but, unfortunately, one of his assistants, Jupille, became seriously ill of Asiatic cholera. Mechnikov, in despair, vowed that he would not survive the death of Jupille. To his relief, the young man recovered and Mechnikov could go on with his research which now provided him with several puzzling facts. He found that in some localities cholera is unknown even when cholera vibrios are present in the soil and water. Some animals were found to be immune to the disease when he infected them with it in the laboratory. Mechnikov explained this by attributing it to alterations in the microbe's virulence. He had previously written in his "Microbial Pleomorphism," in 1888, that such alterations were possible. But what caused these alterations? He was of the opinion that the properties of microbes depend on the bacterial flora in the intestine.

Among the numerous microbe species inhabiting the intestinal tract, some inhibit the development, growth and proliferation of the disease germs, while others (a yeast fungus of the *Torula* type, sarcinae and a genus of the *Bacteria lactici*) are conducive to the growth and proliferation of the vibrio. Mechnikov tested his ideas on new-born rabbits and guinea-pigs, deliberately chosen, because new-born rabbits do not seek their food but feed only on their mother's milk. Their intestines are, therefore, free from microbial flora for a considerable length of time. New-born guinea-pigs, on the contrary, are very active, eat food in addition to milk, their intestines are populated early by micro-organisms. Experiments bore out Mechnikov's conjectures; by introducing cholera vibrios along with their milk, he infected new-born rabbits with typical cholera. The disease ran a more severe course if "favourable" microbes were previously introduced into the intestines. New-born guinea-pigs were infected with cholera only when the vibrio was accompanied by the three types of microbes favourable to the development of the bacillus. This suggested that the epidemiological peculiarity of cholera depended on the complex relationships, existing in nature and within the organism, between the pathogenic agent and other micro-organisms with which it came into contact. The immunity of adult rabbits to cholera and the susceptibility of new-born rabbits may be explained by the fact that the former possess a varied microbial flora protecting them from the infection while the latter's intestines contain no flora.

These investigations were very valuable, as they determined that the outcome of an infection depends, not only on the pathogen and the body's defensive machinery, but also on the microbial environment in which the germ finds itself. Since microbial flora changes in accord with changing environmental conditions and can be changed artificially as well, Mechnikov's work demonstrates once again the relationship between the development of a disease and immunity to this disease, on the one hand, and the external factors and man's interferences aimed at changing or creating a new microbial population (or part of it), on the other hand.

Mechnikov was anxious to solve the most vital problem of the day—that of producing an anti-cholera vaccine. He regarded the neutralization of infection as the essential aim of every vaccination. The chief danger of cholera, its "sting," lies in the product which the cholera germs elaborate, in its toxic action on the body. He was, therefore, of the opinion that, in cholera, hygienic measures would prove more effective than vaccination. The experiments Dr. Shukevich carried out in Mechnikov's laboratory showed that vaccination would not prevent rabbits from dying of cholera when the germ was introduced into their bodies in large doses which caused grave intestinal intoxication. Some Russian bacteriologists, for example, Mechnikov's favourite pupil Zabolotny and his pupils, S. Zlatogorov and P. Maslakovets, disagreed with Mechnikov; they cited their own experience with anti-cholera vaccinations to prove that vaccinations were undoubtedly useful, since they reduced the incidence of the disease and decreased the mortality. When in 1909, Mechnikov visited Prof. Zabolotny at the Women's Medical Institute in St. Petersburg, a heated dispute took place between them, in the presence of other professors and students. The disputants were unable to shake each other's convictions, but the future proved that Zabolotny was correct.

Mechnikov wrote several other works on intestinal flora. He studied the microbiology of diarrhoea in children and discovered that the disease was largely due to the widely occurring *Bacterium proteus*. Among other infections, he devoted much attention to the study of typhoid fever and plague. The subject of his report delivered at the Twelfth International Congress of Physicians in Moscow was "The Progress of Science in Studying and Controlling Plague." He also devoted no small amount of time and

energy to the study of syphilis, the greatest social scourge of the time. Vaccination against this disease proved to be ineffective, but Mechnikov and Roux were able to infect experimental apes with syphilis and to obtain favourable therapeutic results in treating them with calomel ointment. Towards the end of his life, Mechnikov undertook the study of another social disease—tuberculosis. He wanted to find out why it was that people sometimes did not contract tuberculosis in spite of close contact with tubercle bacilli. He explained this phenomenon by postulating that the body underwent a kind of "natural vaccination" at an early age; weakened microbes entered the body from the atmosphere which was replete with microbes, especially in large cities. To verify the correctness of his hypothesis, Mechnikov undertook an investigation of the population on an immense scale. Long ago, it had been observed that no cases of tuberculosis occurred among the nomad Kalmyks in the Astrakhan steppe. But as soon as they moved to town or came in contact with a settled population, they often succumbed to the disease. Mechnikov assumed that the Kalmyks had not been exposed to "natural vaccination" by weakened tubercle bacilli and that was why they contracted the disease in its gravest form as soon as they were attacked by virulent microbes. He proposed to subject all Kalmyks, those living in towns and those living in their usual encampments, to the Pirquet test to establish the presence of tuberculosis infection in the body. In the summer of 1911, the Pasteur Institute sent an expedition headed by Mechnikov (who was 66 years old) and including several Russian doctors, one of whom was L. Tarasevich, a well-known biologist and Mechnikov's pupil, to carry out the tests. It was scorching hot and conditions were extremely difficult, but the results obtained confirmed Mechnikov's conjecture: the Kalmyks were found to have no immunity to tuberculosis and so, when they came in contact with an urban population, they easily contracted the disease which spread very rapidly among them. These data were of particular interest to epidemiology, a science which was just being born at the time. Mechnikov's idea served as a foundation for the present-day preventive vaccination with the BCG strain of tubercle bacillus.

In the last years of his life Mechnikov was not only a theoretical pathologist but also a prominent microbiologist—a master of his science—contributing a number of works possessing considerable practical value.

MECHNIKOV'S STUDY OF OLD AGE AND DEATH. THE THEORY OF ORTHOBIOSIS

> ...Old age is a disease and people should be cured of it.
>
> I. MECHNIKOV

Mechnikov began to study the problem of old age and death at the end of the eighties but its philosophical significance had occupied his mind for a long time previous to that. Indeed, as a youth in search of a "rational" outlook, he was wont to ponder on it. He was haunted by the two frightful spectres of human life—old age and death. When he approached them from the viewpoint of a sober naturalist he saw old age as a dissonance in human nature, the most acute of all the contradictions from which man suffers. He saw that the natural desire to live, not very strongly manifested in youth, becomes stronger with the passage of years and, far from weakening, often becomes extremely strong in old age. In the meantime, however, the process of the organism's physical decay, the process of ageing, continues to fill man with despair at the prospect of life within him ebbing away. Old age signifies the approach of death; the sadness felt at the knowledge that one is old is accompanied by the dread of death. Mechnikov thought that it was this dread of death that gave rise to the idea of the soul's immortality, of life hereafter, of resurrection. What had a man of science, an atheist, to offer in lieu of the lures of religion? Mechnikov offered a twofold solution: as a thinker, he put forward a new, optimistic, theory which, in his opinion, was able not only to explain this greatest of dissonances in human life but to indicate the means of gradually doing away with it, of arranging a well-ordered and happy life—what he called orthobiosis. As a biologist, he attempted to study experimentally the phenomena of old age and death. We cannot accept the philosophical premises on which he built his theory of orthobiosis, nor can it be said that his investigations have completely solved the scientific problem of old age. Indeed, forty years after Mechnikov's death, we are witnessing only the first steps in this study. It was particularly in the study of old age that many of Mechnikov's experiments and hypotheses have proved to be erroneous. But the very idea of studying this vital problem was certainly quite correct and timely. Even here, Mechnikov left traces of his genius and, in examining his work on this subject, we cannot help feeling the impact of his thinking, although we may disagree with him on a number of points.

* * *

Mechnikov considered atrophy the determining characteristic of old age and thought that ageing was the result of atrophy which occurs widely in organic life. He wished to discover the one feature unifying the varied forms of atrophy, only one of whose manifestations is ageing. To do this, he returned to the theory of phagocytosis. From his study of numerous instances of physiological atrophy, he knew that this process took place with the active participation of phagocytes. He had had many occasions to describe this in his work, for instance, the larvae of echinoderms, the autolysis of the tail in the tadpole (as well as metamorphosis in the larvae of flies described by

A. Kovalevsky). Besides metamorphosis, phagocytosis may be observed in other instances of physiological atrophy—in the lysis of the crystalline lens in the underground Proteus, in the uterus regaining its original structure after parturition, etc. Mechnikov paid special attention to the atrophy of muscle fibres in the metamorphosis of the tail of the tadpole (1892). He was able to demonstrate the role played in this process by phagocytes which, in this instance, were represented by parts of the sarcoplasm with nuclei, the sarcolytes which devoured the contractile part of the muscle fibres. Mechnikov asserted that these sarcolytes were able to migrate into the body cavity and become typical leucocytes; on the other hand, he admitted that they could "in certain cases" become muscle fibres. The chief conclusion he drew from these studies was that "muscle atrophy, like some pathological processes in the nature of parenchymatous inflammation, should be regarded as a phenomenon of phagocytosis."

It should be mentioned here, by way of digression, that in this work Mechnikov supported the idea of universal transformation of tissues. At a time when Virchow's dogma of permanent tissue specialization was the accepted teaching, Mechnikov's assertion that tissues were capable of transformation was a distinct challenge. He stated that elements of the muscle fibre could become sarcolytes which, in turn, could become either contractile elements of the muscle fibre or leucocytes. The duty of engulfing and digesting atrophied cells, and even entire organs, was performed by macrophages. He considered them to be a highly varied group of cells consisting of elements of the most diverse origin (blood cells, fixed connective-tissue cells, vessel cells, muscle and neuroglial elements) and resembling one another only in their phagocytic ability. Mechnikov certainly had an exaggerated idea of the role and occurrence of phagocytosis in the organism; some of his assertions of a purely morphological nature were founded on an erroneous belief in the universality of

phagocytosis. The idea, however, that tissues and their elements are transformable and that functional factor determines morphology and behaviour of cellular elements is in perfect harmony with the progressive Soviet histology of today.

Mechnikov believed that the wide occurrence of phagocytosis in the organism was the manifestation of "an inner struggle among cellular elements." (*Forty Years' Search for a Rational Outlook*, 1954, p. 169.)

This was a wrong, naively materialistic conclusion, probably suggested by W. Roux's teaching on intercellular struggle for existence and inner selection. We believe that there is, and can be, no struggle for existence among an organism's cells.

The fallacy in Mechnikov's theoretical premises in no way detracts from his idea of the role of phagocytes in the development of atrophic processes in the organism. He held that, since macrophage activity was a constant menace to the existence of some other cells and tissues, the latter protected themselves from the macrophages by means of specific substances distributed on their surfaces, capable of exercising a negative chemotaxic action on the phagocytes. Clearly, he was unable to say anything definite about the nature of these substances. He saw that the phenomenon of atrophy, implemented by phagocytosis and fairly common even in young organisms, was particularly widespread in old age. In the work under discussion, Mechnikov said, "Old-age atrophy is the result of inner processes going on within the cells . . . of a struggle among tissue elements becoming more intense as the organism grows older." (*Ibid.*, p. 173.) It is the voracious phagocytes-macrophages that triumph in this struggle; old-age degeneration—"macrophagitis"—is nothing more than a disease caused by the intensified activity of macrophages.

What facts were adduced to support this assertion? Mechnikov considered the greying of hair—the loss of pigment—one of the earliest manifestations of old-age atrophy. In a special work written in 1901, he explained this through the activity of the cells in the basal layer of the hair—pigmentophages. They engulf pigment from the cells of the horny layer where the pigment normally occurs and carry it into the deeper layers. He attributed little importance to the explanation which, at that time, was given for the phenomenon of greying—the penetration of air into the basal layer. He thought that the air served to fill cells which had been previously freed of pigment. In attributing phagocytic activity to the cells of the hair (of ectodermal origin), Mechnikov seemingly refuted his own assertion that this ability was the property of mesodermal elements. But he expanded his initial idea of ectodermal cells by stating that, in some coelenterates (such as hydropolyps and actinia larvae), the phagocytes were ectodermal cells. He described a similar picture of neuronophagia in old people and animals. He thought that here the duties of the phagocytes were discharged by cells which were probably not of mesodermal origin—the neuroglial cells—usually regarded as auxiliary elements of the nervous system.

What happens when hair greys or when neurons die through the activity of the neuroglial neuronophages? Mechnikov believed that a similar process occurred in other instances of old-age atrophy; he considered this to be the result of the destructive activity of "anarchic" phagocytes, which had "broken loose" and were acting to the detriment of the organism as a whole.

What was the explanation of the intensification of phagocytic activity in old age? He thought that specialized cells lost their defensive properties and became the prey of voracious phagocytes; the loss of the defensive properties was caused by harmful influences. Mechnikov believed the most sensitive tissues to be the eggs developing in the ovaries, the nervous system and, finally, all "noble" (i.e., specialized) cells. The elements of the connective tissue, on the contrary, were affected only to a lesser degree by the harmful influences, did not undergo the process of old-age atrophy and were even somewhat stimulated, resulting in the replacement of specialized elements by hypertrophied connective tissue. As the organism grew older, the connective tissue underwent a structural, physical and chemical change; it solidified, became calcified and sclerotic. Mechnikov considered these changes characteristic of old age but not the cause nor the determining factor in the process of ageing.

* * *

What were the harmful influences causing the ageing of the organism? He regarded bacterial flora as the most decisive factor.

Mechnikov expressed his ideas of the role of microbes in the process of ageing in full for the first time in a public lecture he delivered in April 1901 at the Literary and Philosophical Society in Manchester on the occasion of the conferment of the Wilde Medal. In analyzing the role of microbes in pathological processes occurring in the organism, he spoke as a convinced evolutionist. "I shall speak of the microbes of the human body in order to prove that the two biological theories of the nineteenth century serve as beacons shedding light on difficult and complex problems, the solution of which has been left to the new century." (*Ibid.*, Academic Collection of Works, 1954, Vol. XIII, p. 177.) The first of the two theories to which he refers is Darwin's doctrine of evolution; the second, Pasteur's teaching on microbes, ferments and disease. Mechnikov then reviewed data concerning microbes making their appearance in man at different stages of his individual post-embryonal development, their distribution in the human body and their occurrence in different animals. He paid particular attention to the numerous microbes inhabiting the digestive tract (shortly after birth, the large intestine contains nearly 45 varieties of micro-organisms); he conceded that, in some cases (probably, rare), microbes could be beneficial, as, for instance, when a young organism has not learnt to elaborate the necessary digestive enzymes (trypsin) or when, as in the instance described earlier, certain microbes, thanks to the phenomenon of antagonism, inhibit the activity of virulent pathogens, for example, cholera vibrio. Mechnikov, however, doubted very much the universality of micro-organisms' beneficial activity and supported his view by pointing out that there are animals—scorpions, the larvae of moth and some other insects—whose intestines contain no micro-organisms but in which the digestive process proceeds normally.

Thus, while intestinal flora may be beneficient, it is definitely harmful. Human intestines contain at least four species of microbes (*Bac. Weltschi, Bac. sporogenes, Bac. putriticus* and *Bac. proteus*) which cause the disintegration of corpses. Their presence in the intestine is accompanied by the elaboration of a series of toxic substances (indole, phenol and sometimes even ptomaine), entering the blood stream through the intestinal walls and causing constant intoxication of the organism. He indicated the exact spot where constantly, drop by drop, the poison intoxicating the body seeped every hour, every moment of its existence. This spot is the large intestine, the part of the digestive tract where the remains of digested food, all kind of residue, are stored and become faeces. The large intestine is the place where the activity of numerous and varied bacteria causes intensive fermentation. Several products of fermentation get into the blood stream and gradually undermine the specialized cells, depressing the activity of phagocytes as well as that of more resistant non-specialized cells, including those of the connective tissue. The constant action of these toxins results in a loss of the organism's most important specialized cells.

To prove his point, Mechnikov cited literary data showing that, with the large intestine isolated (in cases of

fistulas) or when it was artificially sterilized in animals, toxins were not discovered in the blood. He agreed with the opinion of the French scientist, Bouchard, that bacterial flora toxins caused the organism's self-intoxication. Mechnikov considered it very significant that bovine arteriosclerosis (*enteque*) was a result of infectious enteritis from which the animals suffered when young. According to Lignières, this disease could be caused experimentally by infecting an animal with calf cholera. Not content with data taken from books, Mechnikov had undertaken an experimental study of the problem of old age and was in a position to quote the results of his own investigations. With his co-workers Okudo and Draginsky, Mechnikov introduced into the blood of rabbits and guinea-pigs substances produced in the large intestine—paracresol, indole and skatole—and after repeated injections over a period of time, they obtained sclerosis of the aorta and hypertrophy of the fibrous tissue. This represented the first experimentally obtained model of old age. The results of experiments obtained by himself and other research workers enabled Mechnikov to conclude the following: "Although our knowledge is as yet inadequate, we must admit that the flora of our bodies contains microbes which at any moment can become poisonous or facilitate the development of chance pathogenic bacteria and exude more or less dangerous poisons." (*Ibid.*, 1954, p. 189.)

What is the historical and biological origin of this "poison factory" present in our bodies? Mechnikov held that the lengthy large intestine was a "biological disharmony" which man had inherited from his animal ancestors. In mammals, such lengthy large intestines probably facilitated the digestion of vegetable food, particularly of cellulose, with the help of bacteria; such food is assimilated from the large intestine, as for instance, in horses. On the other hand, the possession of lengthy large intestines must have played an important part in the struggle for existence enabling the animal pursued by enemies to run long stretches without stopping to excrete faeces stored in the intestines. But then, it is due to this adaptation that the life span of mammals is much shorter than that of birds, which, in the course of natural selection in order to ensure optimal conditions of flight, developed short large intestines which are often freed of their content—even on the wing. But different birds possess large intestines of different lengths, and, accordingly, have different life spans. Mechnikov was cautious in his conclusion: "We feel much inclined to set this down as a rule: the longer the intestine, the shorter the life." (*Ibid.*, p. 194.) In another place, he writes: "We pay with our suffering for the privileges our ancestors enjoyed from having long intestines populated with variegated flora. This flora is the main cause of the brevity of our lives which come to an end all too early. . . ." (*Ibid.*, p. 197.) But if this reasoning were pursued to its logical end, the fight for a long life would demand surgical removal of the greatest part of the large intestines in children. Mechnikov, however, clearly understood that such an operation was unthinkable. "I presume that nobody would advise an operation to remove the large intestines in order to free the organism of the harmful influence of injurious microbes inhabiting this useless organ." (*Studies in Optimism*, 1907, p. 114.) So his mind began working in another direction. If his assumption that old age was the result of a fight between two groups of cellular elements within the organism was correct, the task of medicine was clear—either to reinforce that group of the combatants which is beneficial to us or to weaken the one which is hostile to us. Mechnikov here recalled the cytotoxic sera and thought that the weakened specialized (particularly neural) elements of the organism could be stimulated by small doses of cytotoxic—above all, neurotoxic—sera. And since embryonic tissues possess the greatest viability, Mechnikov thought it wise to look for anti-old-age substances in embryonic tissues. He believed that weakening

activated phagocytes might yield still better results. This, too, could be achieved by the use of cytotoxic (in particular leucotoxic) sera, but in larger doses, destructive to the macrophages. He envisaged a third, probably the most practical method, that of combating intestinal flora by disinfecting the intestines with different, well-known antiseptic agents, such as ß naphthol, calomel, salol. But the attempt was a failure. His ingenious experiments in weakening intestinal flora with substances capable of dissolving bacterial cell walls (obtained from insect tissues which Mechnikov called ferments and which he isolated from the larvae of the wax moth, or from the alimentary canal of beetles feeding on carrion and capable, under ordinary conditions, of dissolving putrefactive bacteria), were also unsuccessful. In spite of the failure of his experiments, observation showed that putrefactive bacteria died in an acid medium, especially when influenced by lactic acid. This made Mechnikov think of creating a "factory" producing this acid in the large intestine. Here was the familiar idea of biological fight and biological defence which had enabled him to make a number of valuable suggestions for protecting plants from injurious insects. He decided to change the intestinal flora from a wild culture into a cultivated one, beneficial to human health. For this purpose, the large intestine should be populated with lactic-acid bacteria fermenting sugar and producing considerable quantities of lactic acid. After trying a number of microbes of this group, Mechnikov chose *Glicobacter peptoliticus* which converted starch into sugar and for which the large intestine proved a favourable medium, and *Bacillus bulgaricus*. He considered that, by altering the intestinal flora, the process of chronic self-intoxication of the organism and, consequently, the process of old-age atrophy could be retarded. "Man has at his disposal other methods besides natural selection. . . . He can try using his knowledge to establish a harmony of functions with which nature failed to provide him." (*Forty Years' Search*..., 1954, p. 176.)

During the time Mechnikov was absorbed in the problem of old age, he showed himself to be as energetic and indefatigable as before. He formulated practical rules, wrote popular science articles ("A Few Words about Sour Milk," 1907, "Lactobacteria and Their Beneficial Influence on Health," 1911, and some others), supervised the manufacture of *lactobacillin*, a preparation containing lactic acid bacteria in various forms and their enzymes. This last activity caused him some difficulty, because the manufacturers often exploited the name of the great scientist to foist inferior preparations on to the public. Advertisements attributed ideas to Mechnikov which he had never expressed, and often distorted his statements.

Mechnikov perceived that his ideas were being inadequately applied in practice and in the article "Lactobacteria," he wrote (in 1911): "I think it would be a good thing to subject the manufacture of milk ferments by the pharmaceutic industry to as strict a control as that exercised in the preparation of therapeutic sera." He himself was, of course, unable to control the quality of the preparations or the technology of their production—a matter in the hands of privately-owned firms.

In her book, Olga Mechnikova describes a characteristically distressing episode which caused her husband acute suffering. Briefly, it is as follows. When the hygienic role of lactobacteria became common knowledge, a French factory-owner decided to produce preparations containing lactic acid bacteria. He asked Mechnikov to recommend somebody capable of supervising the technology of the process. Mechnikov told him about a young man who had studied the technique at his laboratory and who was in need of money. The manufacturer then applied to Mechnikov to let him use his name for the success of his undertaking. Mechnikov agreed, and the label "Sole provider to Professor Mechnikov" was attached to *Le ferment*, the firm's name. The enterprise flourished but a deluge of difficulties descended unexpectedly on Mechnikov's head. This occurred at the end of 1912 when national chauvinism was on the rampage in France. Right-wing newspapers were persecuting foreigners who "overran" France and "made life hard" for the French, and the great Russian scientist became a victim of this witch hunt. Some newspapers groundlessly accused him of having an interest in the enterprise and only the interference of Roux, Director of the Pasteur Institute, put a stop to this infamous campaign. Mechnikov did not regret having helped the needy family but the unfair accusations rankled. Even if one disregards the chauvinistic slander, one must admit that Mechnikov's attempt to launch a practical fight against the pernicious effects of ageing under the conditions of capitalist society was doomed to failure and could have brought him nothing but disappointment.

* * *

Although he was the creator of the phagocytic theory which enabled him to make major discoveries, Mechnikov was at the same time its slave; often he could not objectively assess such facts which contradicted his doctrine. Today it is clear that he made serious errors in his study of old age. One of the erroneous premises is his assertion that old-age atrophy is a result of phagocytic activity; there is no proof that phagocytes destroy specific elements of the ageing organism, nor is there proof concerning the role of pigmentophages in the greying of hair. Modern histology considers pigment disintegration to be due to the altered nature of nutrition in the tissue. His hypothesis regarding the phagocytic activity of the epidermal cells of the basal layer in hair has found no corroboration, while the connective-tissue phagocytes have been found to play a rather insignificant role. The phenomenon of neuronophagia (the destruction of nerve cells and ingestion of part of their protoplasm by phagocytes) has been found to occur but proved to be of a purely pathological nature and not a manifestation of old-age atrophy of the nervous system. The idea of the struggle between "noble" and "ignoble," or "base," elements of the organism is, in itself, unacceptable and not borne out by facts. Besides, the opposing of connective-tissue elements to all others ("noble") is highly fallacious.

Many and varied are the functions which connective tissue discharges in the organism. Different parts of the skeleton, such as bones, cartilages, tendons and ligaments, consist of specialized connective tissue. This tissue performs a defensive function, acting as a barrier which protects specialized organs from harmful substances and an excess of fluid. In this latter function, not only tissue but also intercellular substances participate, on whose surfaces an excess of tissue fluids and various "scoriae" are deposited. The connective tissue acts as a "plastic," and other tissues are restored at its expense, a scar being the result of regeneration processes—the final stage of inflammation—effecting the replacement of destroyed specialized tissue. Finally, connective tissue has a trophic function; it not only passes on nourishment to organs, tissues and cells and carries away the products of their vital activity, but also controls the distribution of these substances and transforms them.

It is clear, then, that connective tissue is of paramount importance for the body. Indeed, it is so important that it determines, in large measure, the organism's properties and even its outward appearance. The deposition in the tissue of some substances (for instance, cholesterol) results in the pathological condition known as atherosclerosis, while lack of other substances (calcium) results in weak bones—which are also a form of connective tissue. This suggested to Academician Bogomolets the term "the physiological system of connective tissue"; for many years he and his assistants studied the "root of the organism," as he called it, and sought for measures which could be used to stimulate and restore the disturbed activity of this system. Bogomolets's error lay in overestimating the significance of this system and, especially, in believing it to be autonomous, having few connections with other systems of the organism, particularly with the central nervous system. There are, however, numerous data proving that all the activities of connective tissue are controlled by nervous centres. But although many of his assertions are disputable, particularly, that of the universal importance of the "physiological system of connective tissue," yet today nobody questions its great importance, and it is quite clear that Mechnikov was wrong in considering connective tissue an "aggressor" supplanting specialized elements of the body.

Mechnikov's interpretation of the sclerotic process is also unacceptable. Today it is well known that these processes are by no means the result of excessive activity of connective-tissue cells (as Mechnikov believed), but have an entirely different origin. Serious disturbances in the metabolism of tissues result in the deposition of certain substances within them (fat-like substances, such as cholesterol, calcium), which in turn causes sclerosis, scarification, and degeneration of the tissues. His idea concerning the role of chemical intoxication in the process of ageing is also open to dispute; although intestinal intoxication may adversely influence some highly sensitive—above all, nervous—elements of the organism, these influences should be regarded not as the cause but as the effect of the diminished viability intrinsic in old age, particularly, the loss of the power to neutralize toxins produced in the body.

In the course of time, many of Mechnikov's factual data on the study of old age have been rejected or corrected, while his theoretical conclusions have been revised.

And yet, complete rejection of Mechnikov's theory of old age is actually based on a misunderstanding. For instance, he is often accused of presenting a simplified interpretation of the causes of ageing and of the ways and means of combating it. If one is to accept this simplified view, one should consider lactobacteria as the only remedy against ageing: "Eat sour milk and you'll live to be 120 years old," is the formula which, although not directly ascribed to the great biologist, should be accepted as the logical conclusion developing out of such a simplified understanding of his views. But such a conclusion would be a distortion of his idea, for Mechnikov never attributed to lactobacteria, or for that matter, to the altering of the intestinal flora, the role of the sole factor which might help humanity to combat the process of ageing. This is what he writes in the articles mentioned above and which have a somewhat propagandist nature: "I am certain that lactobacteria are of major importance for the purpose of controlling gastro-intestinal disturbances. It should be understood, however, that we do not regard them as a remedy which acts to prolong life or one which combats old age." ("A Few Words about Sour Milk," 1907, p. 31.) And in another article—probably engendered by the unpleasant publicity given his theory, possibly instigated by manufacturers for purely advertisement purposes, he says more pointedly: "In spite of what some journalists have attributed to me ... I have never asserted in any of my works that sour milk can prolong human life; what I said was that, in the premature ageing of our bodies, intestinal microbes play a part, and I advised the use of lactobacteria in order to change the intestinal flora and to retard the process of intracellular decomposition. ("Lactobacteria," 1911, p. 28.) These quotations should suffice to clear Mechnikov of the ridiculous charge of reducing the fight against old age to the use of sour milk. Mechnikov's fundamental error was his underestimation of the social factor which plays the decisive role in rendering the organism prematurely old. A humanist to the core, Mechnikov had only a vague notion that a successful fight against the "dissonances" in human nature was unthinkable without a radical change in basic social conditions. In an essay "Outlook and Medicine," he says: "Orthobiosis presupposes an industrious, wholesome and temperate life without luxury and surfeit. The existing way of life should, therefore, be done away with, as should the extremes of wealth and poverty which today are causing so much suffering." (*Forty Years' Search....*) But the abstract humanism of this scientist was far removed from a correct understanding of social problems. And this at a time when progressive minds in social science were familiar with the ideas of Marx's and Engels' scientific communism!

In his approach to the problem of old age, Mechnikov proved himself to be behind his time. What he did was to "biologize" social problems on the one hand, and to simplify processes occurring in the body, on the other hand.

* * *

His studies of gerontology brought Mechnikov quite logically to the problem of natural death. This is how he defined it: "By 'natural death,' I mean a phenomenon dependent on the organism alone and not on any chance whatsoever." (*Studies in Optimism*, p. 69.) He gave numerous examples of natural death in a variety of plants and animals (rotifers, crustaceans, insects) and expressed the opinion that their death was caused by intoxication of the organism resulting from disturbed metabolism, in particular, a decrease in the intensity of the processes of oxidation. In some cases, for instance in the silkworm moth, death is caused by self-intoxication—urine fills the bladder and is not evacuated.

In studying the behaviour of ephemeras, insects affording one of the most convincing instances of natural death, Mechnikov noticed that shortly before their death, they completely lose the instinct of self-preservation and actually court death, in whatever form.

Mechnikov read a great deal on the subject, interviewed aged people, and arrived at the conclusion that natural death in man either did not occur at all or occurred quite rarely. He thought that this was because the life span had been considerably shortened by the early onset of old age and the numerous diseases which result in death. The comparison of the relationship between the period of growth and the life span in animals with known examples of extreme old age in man enabled Mechnikov to regard 120-140 years (at any rate, 100 and more) the normal span of human life. If man could survive up to this biologically critical age, he would die a natural death; the cruellest "dissonance" of human life would then be eradicated—the disharmony between the instinct to live and the depressing sense of an impending end.

According to Mechnikov, orthobiosis meant living to such an advanced age that the instinct to live gradually weakened, giving place to the instinct to die. Mechnikov persistently looked for proof of this idea in the words of old people who seemed to be willing to end their days and in his own sensations in the last years of his life. It is difficult to remain calm on reading his last diary in which he refers to the weakening of his instinct to live and his calmness at the prospect of death whose approach he felt so clearly during his long illness.

And yet it is difficult to put credence in all that he wrote. Mechnikov was so fond of life in all its manifestations, he loved science so dearly, he did so much for humanity and was so devoted to his intimate friends that he certainly could not have been surfeited with life. And in the light of his own theory, what weakening of the instinct to live could there be (even if allowance is made for the accelerated, condensed passage through life's stages of which he himself speaks) at the age of seventy, long before the time of natural death? This "weakened instinct to live" was largely due to the temperamental instability so common in nervous people and, a bit perhaps, to self-hypnotism—a psychological preparation for the end whose approach Mechnikov, the naturalist, could not but feel. While discarding his assertions about the "weakened instinct to live" (which, it is true, were expressed somewhat hesitantly), we must pay homage to the wise serenity and detached interest of the naturalist, with which he knowingly watched the course of his last disease. All those who witnessed his demise remarked on his wonderful display of calmness, his touching gratitude towards his doctors and friends, and his tender solicitude for the dearest friend whom he was leaving behind—his wife.

If it is not a manifestation of the "natural instinct to die," then it is, nevertheless, a manifestation of spiritual strength, serenity and fortitude which might well be the aspiration for all those who feel themselves to be approaching the end of their life's journey.

Just as in the case with Mechnikov's ideas about old age, we must accept his hypothesis of natural death conditionally. First, because it is presented in mere outline and, secondly, because some of its premises are disputable and require lengthy additional investigation. However, it appears to be obligatory to deal with the problems which were uppermost in Mechnikov's mind during the last ten years of his life and which served as the basis for his favourite philosophical effort—*the theory of orthobiosis*.

The biological essence of this theory can be expressed in a few words: we should strive to prolong human life, to stave off the process of ageing, make old age more physiological, in general, to enable man to pass through a normal life cycle ending in natural death. The realization of this aim can be promoted by the development of medicine which, in spite of considerable recent progress, is still relatively weak in the control of many grave diseases such as tumours, tuberculosis, etc. Equally important is the behaviour of each individual who desires to complete a full life cycle. Such people "should lead a very temperate life and adhere to the rules of rational hygiene," as Mechnikov says in his *Studies in Optimism* (p. 135). The "hygienic rules" require boiled fruits and vegetables and the daily introduction into the organism of pure cultures of lactobacteria to inhibit the intestinal microbes, thus diminishing (or doing away with) the danger of self-intoxication.

The orthobiosis theory, however, cannot be reduced to these biological, or rather hygienic, rules; it lays claim to a more universal philosophical significance, including the sphere of morality and social relations. We will, therefore, consider it at greater length in our study of Mechnikov's outlook.

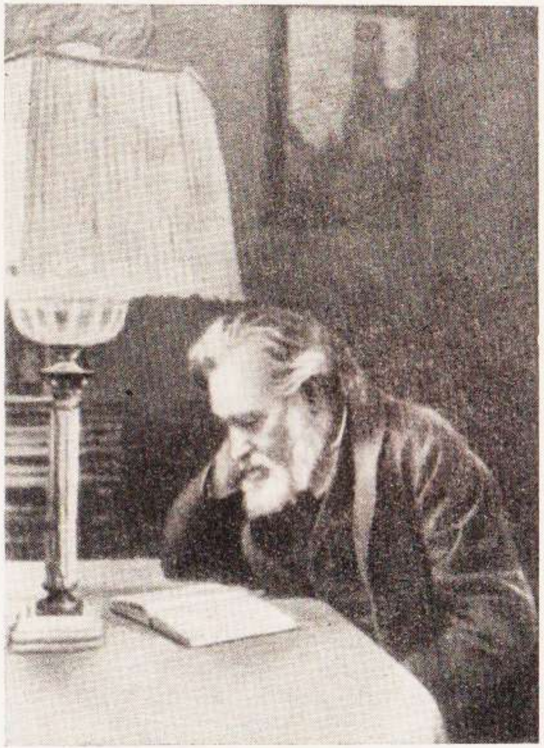
LAST YEARS OF MECHNIKOV'S LIFE. HIS ILLNESS AND DEATH

The first decade of the new century was a happy period for Mechnikov. He enjoyed universal recognition as a scientist, the work he loved so well brought him complete satisfaction, he was happy at his fireside, and his optimism shed a quiet glow on all who came into contact with him.

But life was moving inexorably to its termination and prepared for the great scientist his last ordeal—a long and severe illness—his last opportunity to show his moral strength and fortitude.

The new and alarming note, "the tolling of the bells," as Olga Mechnikova put it, sounded in Mechnikov's house on December 19, 1913, the day on which the scientist suffered his first heart attack—an extremely violent and excruciating one. In *My Observations of Myself*, which Mechnikov began during the attack and conducted with an objectivity astonishing even in a devoted naturalist, he stated that "my heart has been weak from my early youth," and that he had experienced dreadful pains in his

heart at the age of 33. The state of his heart was probably aggravated by the recurrent fever with which he infected himself in 1881 in order to study the course of this disease.



Ilya Mechnikov in 1914—one of his last portraits

His heart continued to give him trouble, beginning with the late seventies; the attacks were sometimes more and sometimes less intense. This, however, did not make him change his accustomed mode of life. In 1911, as a member of an expedition, he went to the Astrakhan steppes where the climate and living conditions were extremely arduous. But the attack on December 19, 1913, put an end to his light-heartedness, the thought of imminent and sudden death haunted him from that time onward. Mechnikov felt a keen interest in observing his own physical state. He was uneasy at the idea of a comparatively early death which would compromise his theory of orthobiosis in accordance with which he had lived for the last seventeen years of his life. Then, too, the thought of his wife's fate after his death gave him no rest. An additional burden was the inability of medicine to cope with a multitude of diseases.

Physically, Mechnikov was fairly well during the spring and summer of 1914; he had no more heart attacks and there was every hope that the disease would take a slow course. But the war proved to be the shock which hastened his death. Mechnikov took it very much to heart; the humanist in him could not accept the sufferings and privation the war was causing mankind. His ideal of a triumphant human mind, his natural aspiration towards a peaceful and happy life were trampled underfoot. He accused the various governments of not knowing how to come to an agreement and of not wishing to do so in order to save their peoples from a blood-bath. He was greatly disturbed over this and, in his letter to the editor of the *Russkoye Slovo* (*Russian Word*) newspaper in Moscow (to whom he sent his article on Pasteur), he wrote about the great injustice of the war a few months after its outbreak. In that letter, Mechnikov counterposed the illustrious forces of science which promoted the happiness of mankind, as personified by Pasteur, to the dark and destructive forces of war. He quoted the words from Pasteur's speech, inspired with humanist ideas, which the great scientist had delivered on the day of inauguration of the institute which bears his name. These words of Pasteur's could well have been Mechnikov's own motto during that period.

Olga Mechnikova reminisces in her book that when she saw her husband after his first visit to the institute after the declaration of war, she "did not immediately recognize him; I saw before me an old man weighed down by an invisible burden." Indeed there was enough reason to despair. His beloved work seemed to be at an end—the Pasteur Institute had been handed over to the military authorities, its staff, with the exception of women and old men, had been mobilized, the experimental animals, including the most valuable apes, had been killed because of lack of food and almost all scientific work was suspended.

News from the front was distressing: some of his young and talented pupils had been killed; the Germans were bombing Paris and bringing death to its peaceful population by aircraft—cruelly ironic chance! called *Taube*—doves. All this caused Mechnikov inexpressible suffering. "It was the war which killed him," his wife states over and over again in her book. He turned for consolation to his work.

During the time of forced inactivity, when no laboratory work could be done at the institute, Mechnikov wrote a book on the three leading lights of modern medicine—Pasteur, Lister and Koch. "It is certain," he wrote in the preface, "that the crazy war which descended on us like a bolt from the blue thanks to the inefficiency or unwillingness of those who should preserve peace, will eventually bring a prolonged period of calm. Let us hope that this unprecedented massacre will long serve to discourage war and strife and will shortly engender a desire for sensible work. Let those whose bellicose ardour cannot cool, turn it not towards war against mankind, but against the enemy consisting of a host of visible and invisible microbes which are striving everywhere to capture our bodies and prevent us from completing our normal life cycle." The book was addressed to the youth and called on them to follow the example of the three great fighters against disease.

It was while the war was raging just outside Paris that the Pasteur Institute celebrated Mechnikov's seventieth birthday on May 16, 1915. Mechnikov regarded these celebrations not so much as a memorable event in his own life but as one having social significance, the glorification of science directed at freeing mankind from war, disease and untimely death.

On that occasion Mechnikov received the following telegram from Ivan Pavlov: "I am proud of experimental medicine. I admire your extensive work of half a century and wish with all my heart that your life and strength may be preserved for many more years of creative work."

The jubilee was celebrated modestly with Mechnikov's close friends and pupils assembling in the library of the half-closed institute. Illness prevented Émile Roux, Director of the Institute, from coming but he sent the warm letter we have quoted several times. Mechnikov's speech in reply to the greetings was devoted to the fight against premature old age and death, to orthobiosis. In conclusion, he said: "When the cares and anxiety we are experiencing owing to the world war have long become a thing of the past, the problems of life and death will still dominate people's minds. Let us hope that the work of our institute, in which I shall no longer participate, will be largely instrumental in enabling human beings to live a normal life span—a span which will certainly be much longer than it is today."

* * *

His jubilee was the last pleasant event in Mechnikov's life. At the end of November 1915, he caught cold but continued to work, commuting daily between Sèvres and Paris. On December 2, he experienced severe heart palpitations but continued work in his laboratory till the 9th. This was the beginning of his last illness which

pursued its course for more than seven months. His basic disease—myocarditis—was complicated by extremely serious attacks of cardiac asthma (which especially tortured him at night), pulmonary infarct, suppurative pleurisy and abdominal dropsy. He bore his affliction with amazing calmness and fortitude. His main interests were the activities of the institute and events at the front; he was particularly interested in news from Russia and welcomed visits from his Russian friends. He continued his self-observations almost to the end, at first making his notes himself and then later dictating them. He attached great importance to them as material to be used in drawing conclusions from the first experiment in orthobiosis.

He knew he was dying and faced death calmly; he hoped he would improve (he did not believe he would get well) in order to be able to supervise the work of his pupils, to act as a kind of "ferment" for them, and to ease the circumstances of his intimate friends—at least, that is what he wrote on May 16, 1916, when he turned 71. On July 15, a day before his death, he said: "All that used to torment me so much, all that seemed so important, now seems so transient, so unimportant, so worthless as compared with the great aims of existence.... Science will settle them some day."

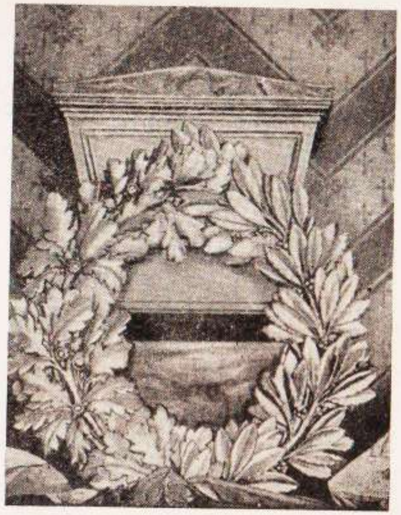
These words are characteristic of his mood at the time. The tinge of sadness in them was occasioned by thoughts about his approaching demise and about his beloved institute where he would work no longer. A few minutes before he died, Mechnikov said to his physician and friend, Dr. Salimbeni: "Salimbeni, you are my friend, tell me is this the end?" He then went on to remind him that the doctor had promised to dissect his body. "Examine my intestines thoroughly. I think they are the most important thing now." A few minutes after that he was dead.

Mechnikov died at 4:20 p.m. on July 2 (16), 1916.

His French colleagues—Roux, Widal, Darré, Salimbeni—were most kind and considerate during all the time that Mechnikov was ill. He felt very grateful to them and it was but natural for him to wish to remain close to the Pasteur Institute even after death. Shortly before his death he said to Roux trying to make it sound as a joke: "Look how my life is interwoven with the Pasteur Institute. I have worked in it for many years; even when I am ill, I am still close to it.... To seal the connection, I think my body should be burned in the oven where experimental animals are burned and my ashes kept in a vessel on a bookcase in the library."

* * *

His wish was respected. On July 18, 1916, Mechnikov's body was cremated at the Père Lachaise Cemetery and the urn containing his ashes was solemnly installed in the library of the Pasteur Institute where it remains to this day.



Urn containing Mechnikov's remains

His long, glorious life, full of creative endeavour, came to an end. But before we finish Mechnikov's story, it would be well to review and summarize his biological, philosophical, and political views. Let us once more call to mind the image of Mechnikov the man.

MECHNIKOV AS A DARWINIST. HIS VIEWS IN THE SPHERE OF THEORETICAL BIOLOGY

Mechnikov occupied a leading place in the fight for Darwinism waged by Russian scientists. His researches in comparative embryology, along with those of A. Kovalevsky, laid the foundation of evolutionary embryology which offered convincing proof of Darwin's doctrine. The basic theoretical premises of Darwinism—the important place assigned to the historical method in the analysis of biological phenomena, the comparative approach to the study of form and function, the interpretation of purposefulness as adaptiveness—found wide application in all of Mechnikov's works, both on biology and pathology. In his article "Darwinism and Medicine" (1910), he cited his "comparative theory of inflammation" as an example of the application of Darwin's principles to a very significant theory in medicine. Mechnikov's attitude to Darwinism was characterized by his desire to assimilate the new teaching critically and to eradicate its errors. He never tired of advocating Darwin's theory; his ardour was wedded to a deep understanding of the very essence of the doctrine.

Mechnikov dealt with Darwinism for the first time in a review of the *Origin of Species* in 1863; but this article by an eighteen-year-old author was not published until 1947. The article, written with youthful vigour, ends in a statement to the effect that although its author considers the theses regarding "biological transformation" as correct, the theory, in its present form, is "untenable." This conclusion is, of course, wrong, but some of the criticism in the article was quite justified. In 1869, Mechnikov published a booklet, *The Teaching of Organic Forms Based on the Theory of the Transformation of Species*, in which he discussed the fundamentals of Haeckel's *Universal Morphology of Organisms*, the first attempt to make this science conform with the teachings of Darwin and Lamarck. While praising this attempt on the part of Haeckel, Mechnikov criticized him for his precipitous, disputable and often erroneous conclusions (the result of Haeckel's vulgar mechanistic outlook and amateurish approach to scientific data), as well as for his propensity for making hasty, yet far-reaching theoretical generalizations.

Seven years later, in 1876, a long article entitled "A Review of the Problem of the Origin of Species," dealing chiefly with Darwin's theory, appeared in the *Vestnik Yevropy* (*European Herald*) magazine. In later life, too, Mechnikov returned to Darwinism. Just as an example, we may cite a chapter in *The Nature of Man*. This chapter is entitled "The Hypothesis of the Simian Origin of Man," and in it, Mechnikov adds comparative-pathological proof to Darwin's comparative-anatomical and comparative-embryological arguments. The proof consisted in the fact that it is quite possible to infect apes with such specifically human diseases as syphilis and typhoid fever.

In 1909, Mechnikov represented the Pasteur Institute at the celebration of the centenary of Darwin's birth at Cambridge where Darwin had been a student. Mechnikov's impressions of the trip and a few thoughts about the connection between Darwinism and medicine are to be found in his articles which appeared about that time in France and in Russia.

This connection was discussed once more in an article "Darwinism and Medicine," written in 1910. Here Mechnikov stated that the experimental study of syphilis and the comparative study of inflammation was made possible due to the application of the fundamental principles of the evolutionary doctrine. He thought that pathology would yield material proof of Darwinism, for example, hereditary changes observable in microbes as a result of external influences or the appearance of new plant species as a result of the activity of micro-organisms. But Mechnikov not only supported and acclaimed the great English scientist, he criticized him as well.

What did Mechnikov find to criticize in Darwin's theory? He considered that Darwin underestimated the influence of environment, a most important factor in the evolution of organisms. In the review he wrote in his youth, Mechnikov remarks: "All these shortcomings [of Darwin's theory.—*S.Z.*] stem from a neglect of the influence which environment exerts on the organism. This undoubtedly constitutes the decisive factor in organization and life. In spite of his knowledge of geology, the author does not pay any attention to nature and the role of changes which occur in the environment." (*Selected Biological Works*, U.S.S.R. Academy of Sciences, 1950, p. 672.) Mechnikov anticipated the views of many biologists of our own time in attributing the decisive role to the environment. He disagreed with Darwin's assertion that evolution necessarily means complication in perfecting the organization of a given plant or animal species. In discussing the question as to whether there was a direct relation between the degree of adaptability of an animal to its environment and the perfection of the organization of its body, Mechnikov stated that there was no such relation: "... In some instances, selection favours higher forms; in others, selection favours lower, and in still others, it completely disregards the degree of perfection and acts in the sphere of properties, regardless of the place occupied in the system."

(*On Darwinism*, 1943, p. 165.) Mechnikov attached much more importance to those physiological properties which are intimately related to the environment—e.g., resistance to humidity and temperature. But the most important factor of all was, in his opinion, fecundity.

It was precisely these important physiological characteristics, and not slight morphological differences (e.g., the structure of the needles in sponges or of the chitinous test in insects) whose adaptive function is not clear, that, according to Mechnikov, made possible the realization of the decisive principle of evolution—divergency.

He also attacked the weakest spot in Darwin's theory—Darwin's overestimation of the importance of overpopulation, and his attributing to it the role of the determining factor in the struggle for existence. It is common knowledge that, in this respect, Darwin was influenced by the reactionary theory of Malthus, so popular in his day.

In his review written in 1863, Mechnikov said: "One of the shortcomings [of Darwin's theory.—*S.Z.*] is the incorrect universalization of Malthus' law and the decisive importance attributed to the principles of natural selection and dying off." (*Selected Biological Works*, 1950, p. 672.) In another place, he wrote: "It is clear to us that Darwin is making a mistake in considering his teaching to be the application of Malthus' law to plant and animal organisms." (*Ibid.*, p. 667.) This is the origin of Mechnikov's negative attitude towards Darwin's debatable idea—the view that overpopulation is the cause of the struggle for existence. As Mechnikov said: "On the contrary, we are inclined to think that the tendency to rapid reproduction is a result of the struggle for existence and not its cause. . . . This tendency or urge, in itself, is not uniform in all organisms as Darwin seems to think; it is a well-known fact that the more numerous the dangers threatening the existence of an organism, the more numerous the means of reproduction it has at its disposal, and *vice versa*."

(*Ibid.*, p. 667.) It should be borne in mind that modern biology, in complete agreement with Mechnikov, holds that the fecundity of a species depends on the conditions of its existence and is the chief factor in its ability to survive.

Mechnikov expressed his disapproval once again of the application of Malthus' ideas to the evolutionary theory in "A Review of the Problem of the Origin of Species" (1876). He saw clearly that an attempt to apply a reactionary social theory with flagrantly colonial character to biology had nothing in common with science. Thus, at the beginning of the chapter dealing with the struggle for existence, Mechnikov wrote: "The ousting of some plants by others has long been known to occur, and this process has been compared with the ousting of primitive peoples by Europeans; the parallel was drawn the more readily since the plants which ousted others were of European origin." (*On Darwinism*, p. 116.)

In opposition to the erroneous and reactionary premise concerning the struggle for existence, i.e., that it is caused by overpopulation, Mechnikov proposed the idea that the struggle for existence in the organic world was varied and, consequently, its causes, too, were different. He expounded this thesis in a popular article, published in *Vestnik Yevropy* in 1878, entitled "Struggle for Existence in the Broad Sense of the Term." This is what he said: "Inasmuch as the struggle for existence embraces a wide variety of phenomena, we cannot confine ourselves to regarding intensive reproduction as the only stimulus in this struggle." (P. 13.)

Unlike the majority of contemporary biologists, Mechnikov did not consider overpopulation the most important factor in the struggle for existence and, consequently, in evolution, and similarly, did not accept Darwin's assertion that intra-species struggle was the chief factor in the process of species formation. To refute this assertion, he quoted the following examples:

"The fallacy of this opinion of Darwin's leads to the untenability of an important thesis advanced by him, *viz.*, that the struggle for existence is the more intense the tighter the organization of the struggling organisms. (*Selected Biological Works*, p. 668.) At another point, he spoke out *against* intra-species struggle: "It even seems to me that similarity in organization of certain beings results in the absence of struggle between them." (*Ibid.*) In refuting the leading role of intra-species struggle in evolution, Mechnikov attached particular importance to inter-species struggle and to competition. In his "Review of the Problem of the Origin of Species," already mentioned, he says: "For the formation of new forms, the intensive reproduction and overpopulation of one form is of incomparably less importance than the coexistence and mutual struggle among many different forms" (p. 122); and on the same page, we read: "For struggle for existence to exercise its modifying influence and, consequently, natural selection, simple overpopulation of one form is not enough; what is needed is competition among the greatest possible number of heterogeneous beings." If it is borne in mind that this was written at a time when the overwhelming majority of leading biologists attached extreme importance to Darwin's theory of intra-species struggle, the originality and daring of Mechnikov's criticism stands out even more forcibly.

He understood perfectly well that the laws of natural selection, so vital in the animal and vegetable kingdoms, were not applicable to human society; it was but natural that he disapproved of the attempts, in vogue at the time, to apply the principles of natural selection to the realm of social relations—an attempt usually connected with veiled—or even open—political reaction.

The ideas Mechnikov expressed in his report "The Progress of Science in Studying and Controlling Plague," presented at the Twelfth International Congress of Physicians held in Moscow in 1897, is very characteristic: "Natural selection, which has created species, loses its power when it comes to human life . . . when it impacts with man, this natural selection is refracted in him as is a beam of light in a prism. It no longer is what it was." This short statement is an effective answer to all attempts to imbue Darwin's theory with reactionary social significance.

* * *

Mechnikov held progressive views, not only in the sphere of Darwinism, but also in many other spheres of theoretical biology, above all, in such important problems as the variability of living organisms and the inheritance of acquired properties. During his numerous experiments with micro-organisms, he often observed that their properties would alter under the influence of altered conditions of existence. Moreover, these alterations were passed on to the progeny even if the factor which had caused them no longer operated. We know that, as early as 1888, Mechnikov published a work on pleomorphism in microbes in which he dealt with the morphological and physiological variability of microbes. He dealt with this in more definite terms in his articles "Darwinism and Medicine" and "Darwin Celebrations at Cambridge," written in 1909 and 1910. In both of these articles, he quoted the same example, one which he considered to be highly convincing. By subjecting anthrax bacilli to the influence of different substances (for instance, chromic and carbolic acids) and high temperatures, Pasteur, Roux and Chamberland were able to change the microbes so radically that they lost the ability to form spores and became non-toxic. Such altered bacilli were used in vaccines against virulent cultures of anthrax bacteria. This change in properties was so stable that it was preserved throughout a long chain of generations after the factor that had caused this change had been removed. Mechnikov repeatedly remarked on the extreme variability of micro-organisms and their ability to pass their acquired properties to their progeny.

We are aware of Mechnikov's opinion concerning a vital problem of theoretical medicine which has recently been justly criticized in our science—Virchow's so-called cellular pathology. In his *Three Founders of Modern Medicine—Pasteur, Lister, Koch*, Mechnikov said: "This formula of cellular pathology, so general as to be almost metaphysical, was unable to penetrate into the domain of medical practice which has remained as empiric as before. In attributing diseases to abnormal modifications of the body's cellular activity, neither Virchow nor his followers have sought to inquire into the causes of such modifications." (P. 9.) From this and subsequent passages, it is clear that Mechnikov disagreed with "localistic" conceptions in pathology and regarded them as a brake on the development of new and correct ideas concerning the essence of pathological processes.

His views on other cardinal problems of pathology, for instance, the etiology and the initial stages of disease, are also worth considering.

The leitmotif of his *Immunity in Infectious Diseases* is the idea that disease is a result of a complex relationship between the macro-organism and the microbe which has gained entry into it.

The achievements of the new science—bacteriology—at the close of the nineteenth century led to a mechanistic theory which was prevalent in medicine, *viz.*, that it was sufficient for a pathogen to enter an organism to inevitably cause a disease, there being no virtual difference between a microbe and the toxin it produced.

Mechnikov took up the cudgels against this simplified approach. He offered numerous instances proving that an organism could tolerate the presence of a microbe (for instance, *Bac. pyocyaneus*) but be highly sensitive to its toxin. This fact alone is enough to show that the relationship between macro-organism and microbe is a complex one. If a microbe does not secrete toxins, its presence may cause no disturbance and may even pass unnoticed. Mechnikov further pointed out that the course of a disease depended largely on the state of the host. This explains the phenomenon of carriers, first discovered by Loëffler, with regard to the diphtheria bacillus. Many bacteria are present in the human body but immunity protects the body from contracting disease. This is what Mechnikov wrote: "In addition to external causes—microbes—diseases are brought about by the inner conditions of the organism itself." These words could be used as a motto for the present-day theories of pathology which hold that the decisive factor in the contraction, as well as in the future course, of a disease is the condition of the organism at the inception of the disease.

It seems clear from what has been cited that Mechnikov was a progressive biologist and thinker.

MECHNIKOV'S OUTLOOK

> If an ideal can unify people and act as a religion of the future, it must rest solely on a scientific foundation, and if it is true that one cannot live without faith, such a faith must be the belief in the omnipotence of science.
>
> I. MECHNIKOV

Mechnikov the man and scientist grew up in the sixties of the last century. It was a glorious period in the history of Russian society, marked by the activity of the revolutionary democrats Herzen, Dobrolyubov, Pisarev and Chernyshevsky, whose influence on him appears to be obvious.

Mechnikov was keenly interested in philosophy and worked out his own outlook. His first attempt at expressing his philosophical views in connection with his biological ideas was the article "Education from the Anthropological Viewpoint," written at the age of twenty-six and published in *Vestnik Yevropy*, in 1871. It was followed by other theoretical articles and, much later, by *The Nature of Man* (1903), *Studies in Optimism* (1907), and *Forty Years' Search for a Rational Outlook* (1913). The first two books were published (in French and Russian) in both Russia and France; the third, presenting the evolution of his theoretical and, particularly, philosophical views, was addressed to Russian readers and written at the request of a progressive Russian publishing house, Scientific Thought, headed by N. Umov, a prominent physicist and Mechnikov's friend.

An analysis of Mechnikov's outlook is complicated, since he was wont to attribute unusual meanings to usual philosophical terms. He characterized his own views as "original positivism" or "sceptical materialism." The first term might suggest that he adhered to agnosticism of which positivism was a variety (propounded by Auguste Comte and his followers), i.e., a doctrine which denied the reality of nature and of the world around us; but as understood by Mechnikov, the term "positivism" implied a rational, positive philosophy, inimical to abstract ratiocinations and vulgar simplification. His peculiar terminology and vague philosophical position came about as a result of his negative attitude towards idealism (which he called "metaphysics" and which he rejected absolutely) and towards mechanistic materialism which discarded development—a philosophy in vogue during the years of his youth (represented in the works of Büchner, Vogt and Moleschott). This latter doctrine Mechnikov aptly defined as "dogmatic" and denounced it as a narrow and hidebound philosophy.

In order to comprehend his philosophical views, it is necessary to ascertain how he solved the cardinal problem of philosophy, the touchstone of all philosophies—the

problem of which is primary—thinking or being, spirit or matter. The answer given to this question divides philosophy and philosophers into idealists or materialists.

Many of Mechnikov's statements make it clear that, for him, matter, nature, is primary, while consciousness is secondary, it being the property of highly-organized matter alone, i.e., of man. This is clear from his polemics with various representatives of idealism, big and small. He was ruthless in criticizing spiritualists, "cosmists" and other "philosophical mystics." He directed a devastating fire of sarcasm against his opponents. Regarding spiritualists, he wrote: "The American philosopher James was so convinced of the existence of a life in the hereafter that he promised his friends that he would find a means of communing spiritually with them after his death. As yet, however, he has not fulfilled his promise." (*Forty Years' Search...*, 1954, p. 26.) He expressed himself in even stronger terms: "When believers in the soul's immortality started evoking spirits from the next world, it was found that the spirits came back in a wretched condition. . . . The above instances of the souls of dead people coming to earth suggest the idea that beyond the grave there is a disembodied madhouse." (*Ibid.*, p. 16.) Mechnikov had the knack of exposing the absurdity of spiritualism. In arguing with the more prominent representatives of idealism, he pointed out the weakest spot in their theory—the idea of the primacy of consciousness and its non-dependence on matter. Henri Bergson, a prominent idealist philosopher, the spiritual leader of West-European intellectuals during the first decades of the present century, wrote in this vein: "Human consciousness must hold an infinitely greater content than the corresponding brain apparatus." And in more precise terms: "Thought, at least for the most part, is independent of the brain." In quoting these ideas of Bergson, Mechnikov said: "All this reasoning, in spite of its seeming profundity and finesse, cannot in the least refute the quite familiar fact that consciousness is affected when cerebral activity is affected and ceases to exist when the latter ceases." In criticizing the idealistic idea of the well-known Belgian writer, Maeterlinck—the idea of the immortality of consciousness and its independence of matter—Mechnikov said: "Consciousness, so intimately connected with our nervous system, is non-existent not only when the nervous system no longer exists, but also when the normal circulation in it is disturbed, which happens in the state of profound slumber, swoon, or under the influence of chloroform or other narcotics."

In Mechnikov's opinion, intuition—creative inspiration to which Bergson attaches such great (even decisive) importance in his philosophical system—undoubtedly depends on matter. As proof of this, he quotes the words of Poincaré, a famous French mathematician, who stated that he had made a significant discovery after he had been stimulated by drinking a cup of black coffee. This example, as Mechnikov said, "shows how a stimulating beverage can awaken creative thought." The statements we have cited—and their number could be multiplied many times—prove Mechnikov's unshakable belief in the primacy of matter and in consciousness being intimately connected with its substratum, brain.

The second touchstone in philosophy is the answer to the question as to whether our consciousness is capable of cognizing the actual world. Mechnikov answered this question affirmatively, saying that, by studying the surrounding objects, we may obtain an objective idea about the existing world, the process of cognition taking place with the help of the organs of sense and thought. True, Mechnikov pointed out that these instruments of sensation and knowledge were imperfect; indeed, he thought they could be compared to an inaccurate balance or an insufficiently precise thermometer, which, however, if used judiciously, can yield valuable data. And he expressed the opinion, in his *Nature of Man*, that even our imperfect

sense organs can lead us to the knowledge of the truth, or of part of it; the correctness of our knowledge is tested by being able to predict the course of events, a property possessed by science alone.

We see, then, that Mechnikov was a materialist, but what kind of a materialist was he? Should we, perhaps, regard him as a mechanist of whom there were so many in his time, especially in Germany? To be able to answer this question, we must recall the peculiarities of his creative activity. We know that the characteristic features of his work were an evolutionary, historical approach to all concrete biological problems; a constant interest in the relationship between the processes occurring in an animal and its evolution (for instance, differences in the mechanism of the inflammatory reaction taking place on different levels of the zoological world); a stress on the decisive influence of the environment on vital processes (for instance, the transformation of the digestive function of phagocytosis into defensive when pathogens invade the host). It seems clear that the narrowness and stability of mechanistic materialism were alien to him; he viewed the concrete facts of his science dynamically, often from the position of elemental dialectics. The nature of Mechnikov's materialism may be deduced even more clearly from some of his philosophical ideas. He emphasized the historical character of the process of knowledge, believing that human knowledge at a given stage in the development of science expressed the absolute truth incompletely, but with the development of science, knowledge came closer and closer to the truth.

Mechnikov's attitude towards vulgar materialism which gave rise to ultra-realism, was uncompromisingly negative. The philosophy, save the mark! of ultra-realism was very simple: it advocated the satisfaction of primitive instincts. The trend which grew up as a reaction to mystical attempts at "becoming one with the universe" held that it was "better to descend to earth and look for all the good which man is capable of doing on earth." But such views, as Mechnikov caustically remarked, "may easily result in behaviour resembling a page in the history of humanity which has been turned over long ago." (*The Nature of Man*, 1917, p. 15.) Such views, typical of the regressive outlook in the period of the decay of capitalism, too, were entirely inimical to Mechnikov.

His ideas about the relationship between science and its practical applications are very important in the characterization of Mechnikov's outlook. To him practical experience was the criterion of the correctness of scientific search. We know that for him, theory was important from the viewpoint of its application to the solution of practical problems facing humanity. While studying the general problems of pathology, Mechnikov strove to see them widely applied to practical purposes, helping to control disease and prolong human life. Even in the initial period of his career, when he was a zoologist, Mechnikov tried to apply his knowledge to practical uses, as is evidenced by his tireless efforts to promote biological methods of controlling agricultural pests. At the same time, while attributing great importance to the practical utilization of scientific data, he opposed vulgar utilitarianism in science, insisting that it is impossible to have every scientific discovery applied immediately to practice.

In assessing biological phenomena, Mechnikov sometimes manifested some methodological vagueness and even showed some elements of mechanism. He denied that the development of biological processes may proceed in leaps and bounds. While studying chemotaxis in lower organisms, he considered this phenomenon *analogous* [my italics.—*S.Z.*] to sensitivity in man and the difference between them purely quantitative. (*Comparative Pathology of Inflammation,* 1950, p. 37.) In this work, he said that "inflammation in vertebrates differs only quantitatively from inflammation in invertebrates." (P. 107.) Mechnikov did not perceive the qualitative difference between the phenomena of inflammation existing at different stages in the evolution of animals.

His thesis that cellular protoplasm possesses sensitivity to external influences is also open to doubt. Yet he attributed to it an exceptionally great importance, considering that this property of cells determined such phenomena as intracellular digestion, immunity, etc. If "cellular sensitivity" connotes ability to react, to respond to external influences, then Mechnikov's ideas can arouse no objection, and some of his examples (the role of sensitivity in various taxes, cytotropisms observable in embryogenesis, etc.) are convincing enough. But Mechnikov went too far and interpreted this sensitivity too broadly and in a simplified way. He asserted, for instance, that the Weber-Fechner psycho-physical law (excitation increases in geometrical progression and sensitivity in arithmetical), was applicable to such phenomena as chemotaxis in the Protozoa and movement and osmotic reaction in plants. (*Comparative Pathology of Inflammation.*) In this way, Mechnikov artificially likened phenomena observable in lower organisms to the psychic sensations of man.

He failed to understand the basic laws governing the development of social relations, the role of the working class in world history, had no faith in a social revolution and the establishment of new ways of life. This political blindness was due to his limitless faith in the omnipotence of positive natural science stemming from the legal enlightenment tendencies in vogue in the sixties, a belief he cherished all his life. This misunderstanding of the basic social laws made Mechnikov a typical representative of natural-scientific materialism.

This is what V. I. Lenin says about natural-scientific materialism in the chapter entitled "Ernst Haeckel and Ernst Mach" in his *Materialism and Empirio-Criticism*, a brilliant work presenting, among other things, a profound analysis of this teaching, "*Natural-scientific materialism* is the instinctive, unwitting, unformed, philosophically unconscious conviction shared by the overwhelming majority of scientists regarding the objective reality of the external world reflected by our consciousness." Lenin notes, however, that what Haeckel "expounds ... is *absolutely* incompatible with any of the shades of prevailing philosophical idealism."*

Lenin concurs in the opinion of natural-scientific materialism expressed by Franz Mehring in his appraisal of Haeckel's book *The Riddle of the Universe*: "He who wants to perceive this inability [of natural-scientific materialism to deal with social problems] tangibly, he who wants to be convinced that natural-scientific materialism must be broadened into historical materialism if it is really to be an invincible weapon in the great struggle for the liberation of mankind, let him read Haeckel's book."**

For all his wisdom, nobility and humanism and in spite of the fact that Mechnikov was more consistent than Haeckel, the naïveté and inconsistency of his philosophical views confined him to the limits of natural-scientific materialism and prevented him from embracing dialectical materialism.

* * *

Mechnikov was sure that, after forty years of search, he had found his own positive outlook and he fought for it with characteristic conviction and passion. As we have stated repeatedly, the cornerstone of his doctrine was his firm belief in the omnipotence of science. In his *Studies in Optimism* (1917, p. 183 et seq.) he stated this frankly, speaking of himself, however, in the third person as "a close friend of mine." But in the introduction to the *Forty Years' Search for a Rational Outlook*, he discarded all disguises. His nervousness, hypersensitivity, and difficult circumstances of his early life (his first wife's illness and death, his conflicts with Leuckart and Markuzen, his lack of means) tended to make a pessimist of him. He bolstered his pessimism by his novel explanation of the important biological disharmonies in human life, e.g., the lengthy period during which a new-born baby is helpless, etc. The young scientist came to the conclusion that "human nature is so wretchedly organized that, after all, living is not worth while." (*Forty Years' Search...*, 1954, p. 38.) He held at the time that the disharmonies of human nature were irreconcilable with the possibilities of human happiness. His erroneous conception was due to his failure to understand social problems; he often confused the concepts, "biological" and "social," attributing the disharmony of the organism to the shortcomings in human nature, while the actual cause was the irrational organization of human society. Thus Mechnikov believed in the existence of antagonism between the mental development and social activity of woman on the one hand, and her functions in the family, on the other. (*Ibid.*, pp. 87-88.)

This tendency to biologize social phenomena is evident in his treatment of the problem which served as the subject of an article written in the seventies—"The Age to Marry." He asserted that the disharmony between the relatively early sexual maturity and the relatively late age at which people marry brings about negative biological and social consequences. But he contradicts his own assertions by admitting that social considerations play a prominent part in this; thus, he says (in *Forty Years' Search...*, p. 65) that "giving a woman in marriage is among the Kafirs a kind of commercial transaction." The same holds true of the numerous examples he cites of parents betrothing babies and even children not yet born. On page 77 he says: "The age at which people marry is determined, first, by financial considerations...." But the causes of such practices as very early marriages and purchase of brides, common in pre-revolutionary times in the Caucasus and Central Asia, were, of course, not biological but social; they were due to the poverty of the mass of the population, the ignorance and backwardness of some and the cruelty and love of gain of others. The history of the socialist state reveals that the disharmony between the ages of sexual maturity and of marriage, as well as many other "biological" disharmonies mentioned by Mechnikov, have disappeared. These disharmonies proved to be nothing other than manifestations of the ugly aspects of antiquated social relations.

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* V. I. Lenin, *Materialism and Empirio-Criticism*, Foreign Languages Publishing House, Moscow, 1952, pp. 361-62, 366.

** *Ibid.*, pp. 371-72.

The five years which elapsed between the last of the pessimistic articles, "Struggle for Existence in the Broad Sense of the Term" (1878), and the introductory speech at the Congress of Naturalists and Physicians in Odessa (1883), brought radical changes in the author's outlook. Mechnikov said that he "had not yet come to a new understanding of the world but his pessimism had paled considerably." (*Ibid.*, p. 39.) In *The Nature of Man* (Introduction to the fourth edition), Mechnikov said: "Human existence is determined by the nature of man, as it exists now, but it would change radically if this nature could be changed." Mechnikov believed that science was to play the decisive role in this matter, so vital for the organization of human life. "Science alone can solve the problem of human existence, and it must, therefore, be afforded the widest possible scope in this respect." Today science has made signal achievements in this sphere. "Positive knowledge—nobody doubts this—brings man new benefits every day." (*Ibid.*, Introduction to the third edition.) To the question as to whether science can make man happy, Mechnikov gave an affirmative answer, bringing into play man's positive qualities. "Whereas among the complex qualities of human nature stemming from his animal ancestors, there are many disharmonic properties causing him difficulties, there are also a multitude of qualities which can ensure him a happy existence." (*Ibid.*, 1907, p. VII.) Science must lay a rational foundation for human life, thought Mechnikov, and as he grew older, his optimism gained in strength until it became the optimistic philosophy of orthobiosis. "What must we do in this world?" Mechnikov asked and replied as follows: "We must bend all our efforts to enable people to complete the entire cycle of life in a harmonic union of sense and mind up to the point when, in extreme old age, they begin to feel surfeited with life." (*Forty Years' Search...*, 1954, p. 18.)

Mechnikov thought that a man's attitude towards life could be influenced by the correct appeal to his consciousness. "Since one's 'feeling of life' can be developed, people's education should be purposefully directed." (*Studies in Optimism.*) He realized that science could not do away with all the disharmonies of human existence at once and said that "in our present misfortune, we have one consolation—in time science will console people in their struggle against the problems which are not yet solved." (*Forty Years' Search...*, 1954, p. 22.) He believed that science would help to overcome disease, to suppress harmful and to encourage beneficial instincts, and to ensure the normal span of human life.

Mechnikov expected science to have the final word in social and ethical problems. As regards social relations, his views betray the narrowness which has been discussed before. He was ignorant of the actual laws governing the development of human society, blind to the complex processes occurring in it (even when they took the form of revolution and shook society, as was the case with the Paris Commune and the 1905 Revolution in Russia), and dealt in naive biological analogies, comparing human society to social insects and even to the Siphonophora colony.

In discussing the intricate problem of morality, Mechnikov tried to connect it with the problem of orthobiosis.

He wrote that "individual morality consists in behaviour conducive to the fulfilment of the normal life cycle." (*Studies in Optimism*, p. 237.) In his opinion, the guiding principle in bringing up a child, in marriage and in all relations with other people, was the need to ensure the fulfilment of the normal life cycle. Based on the principle of doing only that which is healthful, Mechnikov naively advised us never to be angry ("this may cause various diseases"), to avoid luxury, because "luxurious habits are often harmful to health," etc. In speaking about different forms of "ideal behaviour," he came to the conclusion that the principle of self-help would triumph in the future and people would not let anybody do anything for them. He did not deny that, in his theory, morality was determined by egoism, but he believed that the desire to live according to the principles of orthobiosis might be "a potent factor forcing people to live in a community without doing harm to one another, but rather, aiding one another." (*Ibid.*, p. 246.)

He concluded the exposition of his theory by stating that human nature should be changed in accordance with an ideal, its future perfection to be based on precise scientific data concerning the man of the future who would be qualified to follow the precepts of orthobiosis. But Mechnikov's philosophy is not acceptable to Soviet people because it lacks the principle of the universal good, a *sine qua non* for any social and philosophical doctrine.

And yet there is an aspect to the great biologist's outlook that cannot fail to command respect and sympathy—his genuine, wise and calm optimism, particularly manifest in all of his later works.

As N. Chistovich, a pupil of Mechnikov's, writes in his memoirs, the latter's popularity in Russian pre-revolutionary society was due to his ability "to cure disappointment." He preached the omnipotence of science and indeed, it has already solved a number of cardinal problems in the control of disease, the hostile forces of nature and the vicissitudes of life in general. There are problems still to be solved: the postponement of the onset of an old age freed of its ills, and the prolonging of human life to such an extent as to allow the instinct of a surfeit with life (normally present in all of us) to develop and manifest itself. Then humanity will be rid of the thing that oppresses the human mind most of all—the fear of death—and it will look forward eagerly to a long and happy life span. Discussing the possibility of such bliss, Mechnikov says in his *Studies in Optimism*: "Our mind tells us that man is capable of great deeds, and that is why we should hope human nature will change, turning the disharmonies into harmony. Human will power alone can attain this ideal." Elsewhere, he says: "In thinking about his calling, man can never be satisfied with what nature has given him; his own active interference will be required, and just as he has changed the nature of animals and plants, he will have to change his own nature. . . . We ourselves possess that which can turn disharmonious nature into harmonious, one in consonance with our ideal and one capable of bringing us happiness." (*Ibid.*, p. 248.)

Mechnikov addressed his message of optimism to the youth, the most impressionable layer of society, ready to carry on a fight for human happiness, because, as he says in his *Studies in Optimism* (p. VIII), "the experience of those who have lived and worked for a long time may prove to be of use to the youth." He wanted to cure those young people who succumbed to the psychological maladies peculiar to their age. "Young people leaning towards pessimism should learn that their state of mind is transient and that, in accordance with human nature, it will give place to a more optimistic outlook." (*Ibid.*, p. 192.) But he thought that youth should not wait for things to take their natural course and bring about a change in their outlook: they should (at least those who are attracted to positive natural science) participate in the struggle for the elimination of age-old disharmonies of human nature, for the achievement of a happy life in the shortest possible time, as doctors, biologists and chemists. And this sound appeal, equally free of future promises for happiness in life hereafter and of grovelling egotistic utilitarianism characteristic of selfish philistines, did cure pessimism and did introduce young people to an active life, filled with socially useful work. Many a young man, in the years preceding the Revolution, experienced the beneficial curative effect of Mechnikov's optimism.

Soon after Mechnikov's death, L. Tarasevich wrote: "An unceasing search for scientific truth and a constant striving to bring it closer to life and to make it a guiding light, a religion of science, if the word 'religion' can be used about one who denied it—those were the traits which make Mechnikov's personality and strivings interesting and understandable to all, no matter whether one agrees or disagrees with his views."

It is clear to us today that his philosophy was one-sided, incorrect and naive, that he did not understand the importance of social and political ideals in the formation of an outlook. But his wise and sober optimism based on facts and free from groundless illusions—making it all the more invincible—is close to us, to our life-asserting epoch where high ideological principles are not only the foundation of an outlook but the stimulus in our day-to-day struggle for the triumph of life over death.

Mechnikov has left us a behest to fulfil in saying: "The scientist, the philosopher must not regard human nature as it exists today as something immutable, but must strive to change it for the good of mankind. Science will certainly achieve this; we must hope that the new-born century will see this task accomplished." *(The Nature of Man.)* There is hardly anything we can add to this.

MECHNIKOV'S SOCIAL AND POLITICAL VIEWS. MECHNIKOV THE PATRIOT AND THE CITIZEN

Mechnikov was fond of emphasizing his complete lack of interest in politics, his denial, on principle, of any and every form of social struggle. In his "Open Letter to the *Odessa News* Correspondent," he wrote: "You see, all my life has been spent in the laboratory. I shun all kind of political activity, whether Right or Left."

He often spoke disapprovingly and with derision of political activities. In his speech as chairman of the Congress of Naturalists and Physicians in Odessa in 1883, he recommended purging "the ethical pharmacopoeia of *medicamenta heroica* [drastic remedies.—*S.Z.*]." We must admit that Mechnikov's system of political views was often astonishingly naive, inconsistent and not well thought out. But his claim to being indifferent to politics was not in keeping with the facts. Indeed, his whole life was nothing but a manifestation of his warmest sympathies with the ideas of progressive Russian society and of his hate for the reactionary tsarist regime. Furthermore, he participated directly in the political life of Russia. As years went by, the sordid events in the history of Russia in those dark years wrought a definite change in Mechnikov's political and social views. As Olga Mechnikova writes in her book, her husband's attitude towards the situation in his home country changed after his visit to Russia in 1911: "He came into close contact with many facts of Russian reality and they made him turn Left. He was indignant and depressed at seeing free thought trampled underfoot in a country which ought to be particularly solicitous of everything which led to the development of culture." Pure-hearted, kind and noble man that he was, Mechnikov keenly felt oppression, the arbitrary rule of the powers that be and was always in the front ranks of the fighters for justice. The oppression which intensified after 1881 and which consisted in the tsarist government's reprisals against students and the persecution of progressive instructors and professors, aroused Mechnikov's wrath. He expressed his protest by leaving Odessa University in spite of the fact that he liked his work there and was on the best of terms with his colleagues and the students.

Mechnikov explained why he did this in the article, "The Story about How and Why I Settled Abroad," which appeared in *Russkiye Vedomosti*, in 1913. What happened to Mechnikov was to happen again in 1890 to D. Mendeleyev, another great scientist who was also forced to leave St. Petersburg University. Neither of them would tolerate the arbitrary rule in the university, neither would accept the role of unprincipled "pacifier" of the youth assigned them by the university and Ministry of Public Education officials.

The circumstances of Mechnikov's break with the university in Odessa are important not only biographically, but also as a manifestation of the academic life of the period. The teaching staff at Novorossiisk University was split into two clearly defined parties—a reactionary, consisting of the mathematicians Yaroshenko and Sabinin, the law professors Patlayevsky, Malinin, and some others, and a progressive party to which Mechnikov, Kovalevsky, the economist Postnikov, the chemist Verigo, the historian Uspensky, and others belonged. Life afforded numerous occasions to express their differences of opinion, and the impetuous and impatient Mechnikov was always in the lead, voicing his opinions concerning principled as well as non-principled questions. He voted to place the university auditoriums at the disposal of women's higher courses; he was elected to the board of the society of needy students, he argued for sending university representatives to scientific congresses held in Russia and abroad, and so on. It is easy to see that Mechnikov's active participation in social life, his unpretentiousness and accessibility to junior instructors and students could not but irritate the dry-as-dust and conceited "high priests"—or rather officials—of science, his colleagues, who treated students coldly and suspiciously and jealously guarded their professorial dignity.

Things became much worse after 1881. Following the assassination of Alexander II, Russia became the scene of unbridled reaction. A wave of repressions swept the universities, destroying the last remnants of their autonomy and crushing the students and progressive professors. In the middle of that year, beginning with Professor S. Yaroshenko's appointment as rector, the atmosphere at Novorossiisk University became very tense. A symptom of the "morbid state" of the university, as M. Shpilevsky, one of the progressive professors, termed it, was the "November incident" which, briefly, was as follows:

When Professor Patlayevsky, Dean of the Department of Law and an inveterate reactionary, examined the theses for the Candidate of Law degree, he discovered that one thesis, written by the talented young scientist, M. Herzenstein (afterwards a member of the First State Duma who was murdered by the Black Hundreds in 1906), contained "socialist tendencies," and suggested that such theses be refused a hearing as a matter of principle. The members of the faculty who were, for the most part, reactionaries, supported the Dean's proposal directed not so much against the young candidate as against his teacher, Professor A. Postnikov, who was very popular with the students. The decision labelled Postnikov as politically unreliable and was nothing but a disguised denunciation. The students learned about the Dean's proposal and its approval by the faculty from some progressive professors, including the indifferent to politics Mechnikov, and on November 20, 1881, they carried out a protest demonstration against Patlayevsky on the university grounds. The university tribunal expelled several students, including one who, as

Mechnikov attested, had not even participated in the demonstration. This led to more and stronger protest. The unrest among the students assumed larger proportions, and the inspector of education decided to take special measures. He invited Mechnikov and a professor of the department of history and philology and asked to persuade the students to desist from calling meetings and demonstrations and to resume their studies. The professors promised to do what they could but stipulated that, after the restoration of order, Professor Patlayevsky should resign his deanship. The inspector agreed to this condition, the students heeded the appeal of their favourite professors and studies were resumed. But the official reneged on his promise "on the pretext," according to Mechnikov, "that he was a simple official obeying the orders of his Minister and incapable of making his own decisions." (*Pages of Reminiscences*, p. 83.) On February 3, 1882, Nikolai, the Minister of Public Education, addressed a letter to the professors of Novorossiisk University, brusquely threatening with reprisals those who "corrupted the students' minds." We find the following in the *Transactions of Novorossiisk University*, Vol. 35, pp. 40-41, 1883: "His Excellency deemed it his duty to say frankly that by founding and financing universities, the government provided for the higher education of the youth, but that this solicitude could not be separated from its desire that the youth while receiving the higher education should be free from corruption; indeed, protection from corruption is a no less sacred duty than the conferring of the benefit of mental development. The government has the right to expect teachers of the university to serve it not only by delivering lectures in various branches of science but also by inculcating upon their audiences—both by word of mouth and personal example—those principles of high morality, respect for law and order, which are primary civic virtues. Any deviation from this road and any lack of unanimity in its pursuance would shatter the confidence the government reposes in the learned staff as a body and in each of its members individually; should disorders occur again, the government would be faced with the painful duty of looking for the roots not only in the midst of the hot-headed youth but also amongst the professors' corporation as well."

Such was the letter that caused the cowardly official to break his word. At the same time, it prompted Mechnikov to leave the university, an act he had been contemplating for some time. It was by no means easy for him to take this step—to leave his beloved work—and a few months elapsed between the events described above (February 1882) and the tendering of his resignation (May 1882). Each of his friends accepted the news in his own way. Thus Kovalevsky pleaded with Mechnikov to remain at the university: "I learned with dismay that that nasty business may result in your leaving Odessa University. It would be a terrible blow to the university and would just suit those forces against which you have been fighting." In a letter of April 14, Sechenov wrote to Mechnikov: "I have heard about your intention to leave the university; of course I think this quite normal, but, naturally, I curse the conditions which put a man such as you are beyond the pale." As to Mechnikov, he continued his public condemnation of the reactionary policy of the Ministry of Public Education frankly and openly. One such occasion presented itself when, in April 1882, the new Regulations Concerning University Inspectorate were to be discussed. These regulations were an attempt to introduce into the universities a police regime and to deprive the professors' councils of the few rights in the management of the universities which they still enjoyed. Mechnikov spoke on this vital problem at the council on April 22. He reconstructed the November events in detail, dwelt on the role the council had played and said in conclusion: "This incident, accompanied by extremely distressing events, was followed by grave consequences which may affect the fate of Novorossiisk University as a whole."

In the meantime the students learned about Mechnikov's intention and the plans of other favourite professors to leave the university. On May 15, a letter signed by 95 students was sent to Professor Yaroshenko, the Rector. It is a document astonishing by virtue of its mixture of courage, high principles and childish naïveté.

"After a year of your rectorship, a year filled with misunderstandings and conflicts, the affairs of the university directed by your hand have developed to such a point that the professors who were formerly the university's pride, are obliged to leave their posts. The decision of Preobrazhensky, Postnikov, Mechnikov and Gambarov to resign has stunned all of us, and probably all the professors as well as yourself. We wish to believe that these regrettable results have come to pass in spite of your wishes, that they are the unhappy consequences of the spirit in which you have conducted the affairs of the university, intending everything for its good. But they must convince you—as they have finally convinced us—that your direction is harmful to the university. We therefore expect you, in order to prevent the misfortune of the university losing its best professors, to resign your rectorship."

It is of interest to know that, among the signatories, there were young men who later became leading lights in science, such as Academicians N. Zelinsky and N. Andrusov, Professor A. Manuilov, Rector of Moscow University, the bacteriologist V. Khavkin, the founder of the famous Bacteriological Institute in Bombay.

Yaroshenko gave the authors of the letter short shrift: at a special meeting of the council held on May 3 in the absence of progressive professors, a decision was adopted to expel seven of the "culprits" and to reprimand the rest.

After this, Mechnikov decided to act promptly and on May 22 the council considered his resignation. Progressive professors, hoping that things might right themselves

and that Mechnikov might be talked out of his decision, proposed at the meeting of the council to postpone considering Mechnikov's resignation till September; their proposal was however voted down (8 to 7) and the council decided "to support Professor Mechnikov's resignation." Three professors, F. Shvedov, a physicist, V. Ligin, a mathematician and A. Verigo, a chemist, reserved their opinion, which enabled Mechnikov's supporters, a week later, to make one more attempt to dissuade him. It was on May 31 when, at a regular meeting of the council, their reserved opinion was made public, as was the custom, and the question was put as to whether the council desired to change its original decision.

Three professors expressed their opinion in written form as follows:

"Inasmuch as the majority of the council has decided to support Professor Mechnikov's resignation, we have the honour to submit the following considerations:

"Professor Mechnikov's services to science and his pedagogical talent are such as to make it imperative for the university to employ all measures at its disposal to keep him on its staff. Yet the council, without resorting to any measure whatever, promptly decided to support the said professor's resignation. Such haste is unjustifiable. The reason given in the resignation is weak health, but then who of us is perfectly well? But we all hope to regain our health sufficiently during the holidays so as to resume our work. It is quite possible that during the holidays the health of our respected colleague will so improve that he will be able to continue his useful activities. To attempt this first measure is the duty of each member of the council who has the interests of the university at heart. There are some who object, saying that Professor Mechnikov has not authorized us to do so. But the question concerns not his interests but those of the university and for that we do not need any special authorization.

"In view of the above, we propose that the decision to support Mechnikov's resignation be postponed till the end of the holidays and be considered at the council's first meeting in September."

When this was put to a vote, 9 members were in favour of the original decision and 8 against. Although the result seems fortuitous, as the decision was passed by a majority of one vote, Mechnikov's removal from the university was a foregone conclusion. This is clear from the subsequent course of events.

Mechnikov's resignation was accepted within a few weeks—an alacrity quite unusual in the Ministry of Public Education which might justly have been called Ministry of Procrastination. But the reason for such astonishing haste is now well known, as a result of the discovery of a very interesting document in the archives. This is the letter from the Odessa area inspector of education to Minister Delyanov in which the inspector recommended accepting Mechnikov's resignation as quickly as possible since he exercised a pernicious influence on the students, and his removal from the university would be highly desirable. The letter bears an inscription in Delyanov's hand: "To be kept in a separate dossier."

We learn of Mechnikov's feelings at that time from the letter he wrote to Kovalevsky from Messina on January 19 (31), 1883. "On no account will I have anything to do with Novorossiisk University until a radical change has taken place in the conditions which made my stay there so painful that mere recollection of it makes me shudder. But since your own letters show that the bad conditions at the university are likely to become still worse, there can be no question of my working either at Novorossiisk or at any other university. I should be greatly surprised if the new regulations you mention do not result in the resignation of those professors who have the least possibility of leaving." *(Pages of Reminiscences,* p. 229.)

The episode just described illustrates that Mechnikov's assertion that he refused to be interested in politics was not warranted by facts. His behaviour in this conflict may have been naive, he may have shown himself to be too trusting, but he acted as a representative of the progressive, even revolutionary, section of society. A democrat and lover of freedom at heart, Mechnikov hated the reactionary regime of Russia all his life and said so on more than one occasion. His hostility to the life in autocratic and plutocratic Russia made him leave Russia for good soon after his breach with Odessa University; it made him refuse all proposals to come back on more advantageous terms. The first of these proposals was made to Mechnikov in 1888 when he was contemplating settling abroad. At that time, an institute of experimental medicine was about to be organized in St. Petersburg. As can be seen from N. Gamaleya's letter to Mechnikov, the patron of the institute, the Prince of Oldenburg, wanted to have him at the head of the new institution and was ready to accept all the conditions Mechnikov might offer. "He (the Prince) says he will do anything you want—just to have you in Russia." Mechnikov, however, refused this proposal, for conditions in Russia were such that the Prince might break his word (or be required to break it) just as had been the case with the Odessa inspector.

A second and very insistent attempt to induce Mechnikov to return to Russia was made much later, in 1913, in connection with the death of Professor V. Podvysotsky, Director of the Institute of Experimental Medicine. Mechnikov was not only offered the directorship of the institute, he was to head all scientific work in biology and medicine in Russia. In a letter to Mechnikov (dated February 4, 1913) his pupil and intimate friend Daniil Zabolotny asked him in very moving terms to become "the guide of all scientific forces in Russia." Although the Prince of Oldenburg did not invite Mechnikov, fearing that he might refuse again, he was ready to sign the appointment order and scientific circles awaited the great biologist's decision with eagerness. But Mechnikov refused and in such terms as to make his refusal sound like a demonstration of protest against the policy of the tsarist government. In addition to a letter to Zabolotny (which was to be widely circulated among scientists), Mechnikov gave an interview to the Paris correspondent of *Vestnik Yevropy*, which appeared in the June issue of the magazine (1913), and threw light on the negotiations.

Mechnikov dwelt particularly on one aspect of the tsarist government's policy—discrimination in the acceptance of Jews into state institutions. He mentioned the names of his pupils, such as Bezredka, Volman and Bardakh, and pointed out that Bardakh was not invited to work at the Institute of Experimental Medicine in spite of his teacher's—Mechnikov's—ardent support. But national policy was not the only point that drew Mechnikov's fire. He said: "You may not be a Jew, you may be a gifted scientist and yet be left beyond the pale." And he went on to say: "In studying the activity of the Ministry of Public Education, I have come to realize that it is directed towards the detriment of science in Russia. . . . That is why I deem it best to remain in Paris where my laboratory is open to all Russian scientists who desire to work and who can work. Here with me, they are at home."

The political significance of this public statement of Mechnikov's is clear from the correspondent's accompanying remark: "Russian readers will perceive the bitter irony of such a state of affairs when a famous scientist can better serve the interests of Russian scientists and of science in Russia by staying abroad than by becoming the head of a Russian scientific institution."

In his letter to Zabolotny, Mechnikov again repeated that he was inimical to all politics and added: ". . . but I could not be present and calmly observe the destruction of science now so cynically perpetrated in Russia."

This clearly shows that Mechnikov was intolerant of baseness and oppression and at the same time refutes his own assertions of being indifferent to politics.

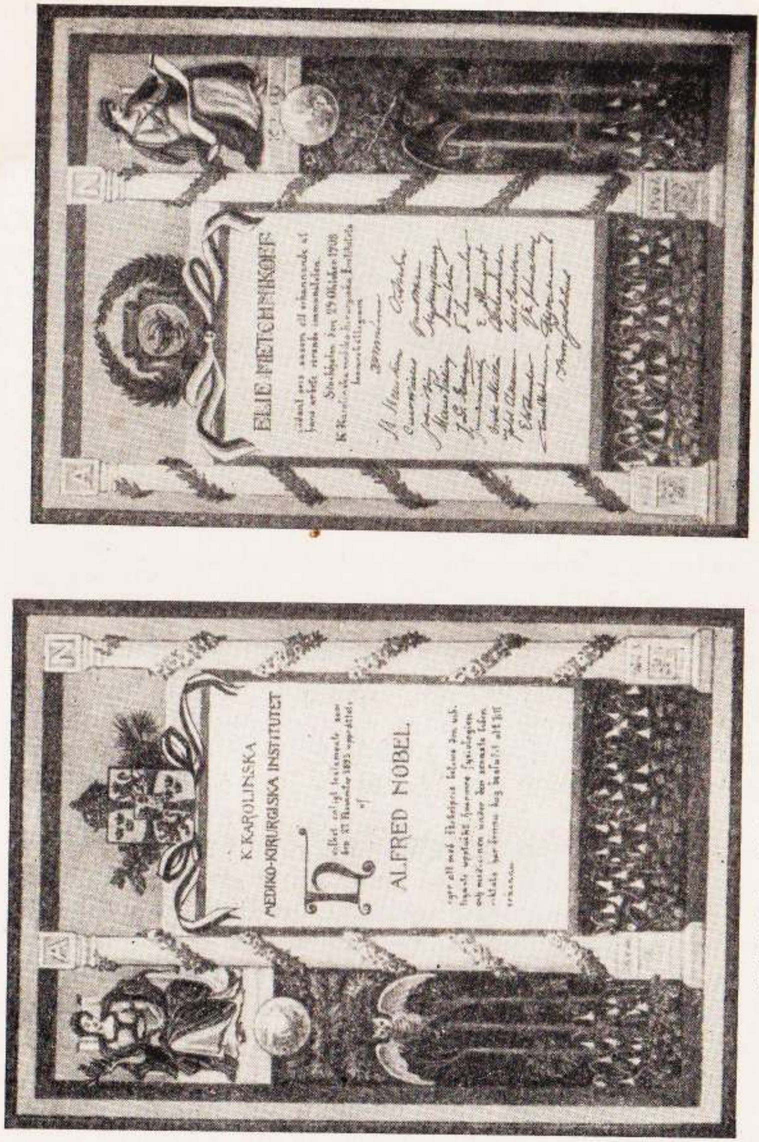
Living outside of Russia, Mechnikov preserved his personal and scientific ties with her. He contributed articles on the results of his experiments to Russian scientific journals (especially to *Russian Archives of Pathology*), wrote philosophical books, one of which, *Forty Years' Search for a Rational Outlook*, was written at the request of the progressive publishing house *Nauchnoye Slovo* (*Scientific Word*) for Russian readers, and a series of autobiographical and biographical articles, including "The History of Biology in Russia in the Last Fifty Years," "The Story about How and Why I Settled Abroad," "My Stay in Messina," reminiscences of A. Kovalevsky, I. Sechenov, N. Pirogov, N. Umov, L. Pasteur, J. Lister and R. Koch.

One detail may serve to illustrate his regard for Russian society: in the preface to the Russian edition of his *Studies in Optimism*, he makes the following remark: "The feeling that my readers will appreciate prompted me to omit mentioning in the French edition that my critics were my compatriots." (*Studies in Optimism*, 1907, p. VII.)

Admiration for his compatriots was expressed in Mechnikov's article "The Law of Life" (1901): "A constant search for the truth of life, a striving to act in conformity with basic theoretical principles have long constituted a most characteristic feature of the Russian spirit."

The broad strata of Russian society repaid Mechnikov with love and respect, taking pride in him and considering him a man who had won honours for Russia in world science; they never ceased to regret the fact that a great Russian scientist was forced to live and work outside of his own country.

After settling in France, Mechnikov visited Russsia four times. In 1894, he came to Kiev to study cholera during



K. KAROLINSKA
MEDIKO-KIRURGISKA INSTITUTET

ALFRED NOBEL

ELIE METCHNIKOFF

Nobel Prize diploma awarded to Mechnikov for research in immunity

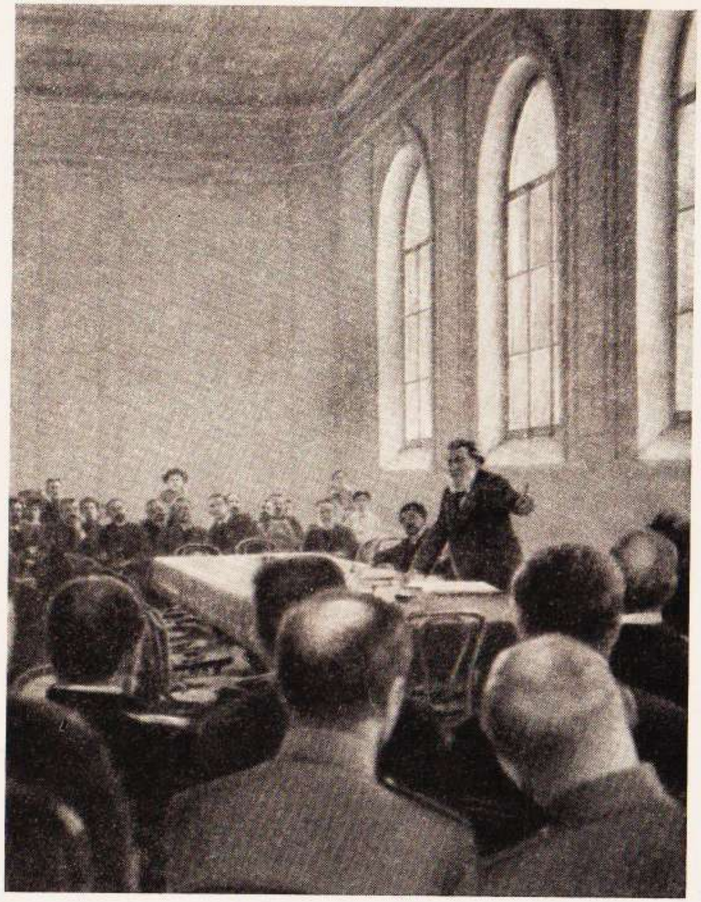
the epidemic; in 1897, he attended the Twelfth International Congress of Physicians in Moscow; in 1909, he visited Moscow and St. Petersburg where he delivered reports, and in 1911, he was a member of an expedition studying the spread of tuberculosis among the nomadic Kalmyks in the Astrakhan steppes. The esteem in which Mechnikov was held manifested itself with particular vividness when he came to Russia in 1909 from Stockholm and delivered the speech of the Nobel Prize recipient, entitled "The State of the Problem of Immunity in Infectious Diseases Today."

A group of Russian scientists, headed by D. Zabolotny, President of the Microbiological Society, had asked Mechnikov to come to Russia and deliver lectures and reports on his latest work. He came accompanied by his wife and remained in Russia for about three weeks. The reception accorded Mechnikov at that time constituted an uninterrupted succession of triumphs.

On May 14, 1909, a session of the Microbiological Society was held in the Assembly of the Nobility (today the building of the Philharmonic) in St. Petersburg; all the biological and medical societies of the Russian capital, as well as representatives of the municipal administration, physicians and student youth, participated in the session. The hall seating 2,500 was filled to capacity. Mechnikov intended to speak on a specific topic: "Investigations of the Cholera Vibrio Conducted at the Pasteur Institute," but when he realized that a large number of non-physicians were present at the session, Mechnikov decided to broaden his theme and spoke on the study of cholera in general.

As usual, Mechnikov's report contained rich material, was brilliantly presented and aroused the enthusiasm of his audience. It called forth a demonstration in honour of the great Russian scientist doomed to live and work abroad and against the government and all reactionary forces. In his speech of welcome, Ivan Pavlov, chairman of the session, expressed his appreciation of Mechnikov as a representative of Russian science. He said: "We cannot but take pride in the fact that Ilya Ilyich Mechnikov is a Russian by birth. After the defeat experienced at the hands of outer and inner foes alike, Russian intellectuals need faith in themselves. They can draw this faith from the knowledge that in the person of Ilya Ilyich, the world has recognized the power and potency of the Russian mind—calm, profound and objective." After Mechnikov's report, there were speeches by N. Rubtsov, the mayor, V. Hubert, President of the Society for the Preservation of Public Health, N. Velyaminov, the surgeon, K. Rauchfuss, the pediatrician, V. Bekhterev, the well-known psychiatrist and neuropathologist, V. Shimkevich, the zoologist, and many others. All expressed their regard for the outstanding scientist and regretted that he was only a visitor in Russia. In the addresss presented to Mechnikov by psychiatrists they wrote: "Sharing the joy of the Russian physicians at seeing you amongst us today, we think that we will not be mistaken in saying that we also share the regret of all Russian intellectuals at seeing you in the front ranks of scientists not of your own country which failed, in its time, to keep you." The *Collection*, published specially on the occasion of Mechnikov's visit to Russia, carries a detailed description of the festivities in his honour. Among other things, it says that: "The official representatives of the Ministry that should lead the activities in honour of Mechnikov are conspicuous by their absence. It has learned no lesson from the example of a genius misunderstood and cast out by the stagnant Ministry of Public Education and has not hastened to make amends for its unpardonable sin. True to the principles of its old system, on the very day of festivities, it probably continued, in its offices, to hatch new plots against Russian talent destined to flourish on foreign soil. . . ." (P. 82.)

Mechnikov stayed in St. Petersburg until May 25;



Ilya Mechnikov speaks at the joint session of scientific societies held in his honour in St. Petersburg during his sojourn there, he visited different medical institutions, acquainted himself with anti-cholera investigations and participated in a number of scientific sessions and disputes (on controlling cholera, recurrent fever, etc.).

He was elected Honorary Member of many scientific societies and educational institutions: the Society for the Preservation of Public Health, the Peter Agricultural Academy, the Psychoneurological Institute, the Society of Naval Surgeons in Kronstadt, and many others. The Military Medical Academy (former Medico-Chirurgical) conferred upon him the title of Doctor of Medicine *honoris causa*; the document proposing to grant the doctor's diploma to Mechnikov bears the signatures of such famous scientists as I. Pavlov, N. Kravkov and V. Bekhterev.

On May 26, Mechnikov arrived in Moscow where he was honoured at many functions. On that same day, a joint session of the Society of Lovers of Natural Science, Anthropology and Ethnography, of the Society of Explorers of Nature, and of the Medical Societies of Moscow, was held in the large auditorium of the Polytechnical Museum which was filled to capacity. Mechnikov reported on "The Flora of the Intestinal Tract" and listened to speeches of welcome from 34 scientific societies, educational establishments, hospital staffs, students' scientific societies, newspapermen, etc.; the address from Moscow University, read by its Assistant Rector M. Menzbir, a well-known zoologist, was of particular interest. Among other things, he said: "If today the voices of physicians are heard with special clarity among the chorus of greetings to you, this does not mean that biologists have forgotten your outstanding works on embryology written in the seventies and eighties of the nineteenth century. The generation to which I belong learned zoology from your books and those of A. Kovalevsky, and to this day we turn to them for advice gratefully. Your sober voice, heard in the orgy of Haeckel-worship, always brought us back to strictly scientific research and warned against tempting but unfounded generalizations."

After the session, Mechnikov stepped outside and found himself on Lubyanskaya Square surrounded by an immense crowd of youth who welcomed him with an ovation.

In Moscow, too, Mechnikov visited different medical and other institutions, such as the Rublyov water-supply system, the Bacteriological Institute, the Cancer Institute, the Higher Women's Courses, etc. He was ready to give advice everywhere and in general acted as one who had the interests of public health and education in Russia close to his heart.

On June 1, the Mechnikovs left for France. Here is the letter Mechnikov published in *Russkiye Vedomosti*:

"I cannot leave for France without expressing the feeling of deep gratitude which fills my heart at the unusually warm reception I was accorded in my native country. Wherever I went—Petersburg, Moscow, Kronstadt, Yasnaya Polyana—I was made welcome and this welcome fills me with a joy I will never forget. Not only scientific societies and other institutions related to science, as for instance, the universities, the Bacteriological Institute, etc., but also the town councils of St. Petersburg, Kronstadt and Moscow, and persons not belonging to the learned fraternity, all were most kind and attentive, the memory of which I will cherish for the rest of my life. Not being a good speaker, I was unable to express my feeling of gratitude with sufficient eloquence after all these speeches and toasts. Not possessing any literary gift, I am at a loss for words to give vent to the feelings that fill my breast. But I hope that these simple lines will, nevertheless, reveal the sincerity and depth of my emotions." (*Collection*, p. 112.)

Mechnikov's visit to Russia showed the strength of his ties with his country and the love which the progressive intelligentsia felt for him.

He proved himself to be a sworn enemy of reaction, and the tsarist government naturally regarded him with suspicion. The Police Department listed him among the suspect and a file was started at the secret police dealing with the "doings of ex-Professor Mechnikov." All his activities abroad, all his ties, personal or professional, were closely watched by the Russian secret police. His sympathies were with the common people, student youth and working intellectuals whom he respected for their high ideological principles, selflessness and devotion to science. After his trip to the Astrakhan steppes he spoke with admiration about the little-known intellectuals who were working under the exceedingly difficult conditions prevalent in remote districts and who constituted a great cultural force in Russia.

L. Tarasevich, a pupil of Mechnikov's, later said that, during his last and fatal illness, Mechnikov evinced a passionate interest in news from Russia and called upon his Russian friends to keep up their hope for a better future, to keep a stout heart and to continue to work.

Mechnikov died nearly a year before the Great October Socialist Revolution which opened up broad vistas before science. We can only imagine with what enthusiasm Mechnikov would have worked had he lived under the conditions existing in the Soviet state. We believe that he would have welcomed the Revolution with as much sincerity and have served the young Soviet country with as much devotion as did his like-minded friend, Kliment Timiryazev.

MECHNIKOV THE MAN AND TEACHER

In Mechnikov, the scientist and the man were blended into a harmonious whole. That he was no ordinary man is evident from the recollections of all who knew him either intimately or slightly.

Mechnikov's temperament was a striking trait: if he was interested in some scientific or social problem, he devoted all his energies to it, he became engrossed in it to the exclusion of everything else. In his *Observations of Myself*, he wrote that he had passed an accelerated life span because all his life he "had been excited, always on the point of boiling." He spared no effort in his service to science, he risked his very life. Twice he infected himself in order to test the correctness of his ideas. The first time was in Odessa when he injected the blood of a person suffering from recurrent fever into his blood to see if this would transmit the disease.

He contracted a severe form of recurrent fever which seriously affected his heart. The second time was in 1892, when he infected himself with attenuated cholera vibrio.

Mechnikov's temperament was also revealed in the pertinacity with which he fought for his scientific ideas. We know how persistently and consistently he fought for his phagocytic theory which has now held undisputed sway in science for several decades. He was free of petty vanity, often observable in certain famous scientists, preventing them from openly acknowledging their errors. When Mechnikov made a mistake, he openly admitted it; he was in the wrong in his disputes with Kovalevsky, Ehrlich and Vysokovich, and he said so.

* * *

Mechnikov was an unexcelled mentor to young scientists. This is what his favourite pupil, Bezredka says: "He was a born teacher; he had a singular approach to the youth and knew how to implant love for experimentation in their souls; he would encourage a tyro at the moment of his dejection and curb his ardour when his imagination threatened to run away with him. He did all this imperceptibly, never wounding young ambition, with a fatherly smile in his kind eyes." (*Recollections of Mechnikov, Priroda,* Nos. 7-8, 1926, p. 42.)

As L. Tarasevich said: "In his love, his passion for science, lay the secret of Mechnikov's influence on those around him, the secret of his importance as a teacher."

The great scientist was exacting of himself and his co-workers, intolerant of falsehood, free from class, national or caste prejudices. He considered all manifestations of chauvinism an unpardonable sin. While in Odessa, he supported Professor A. Verigo, whose election to the chair of chemistry reactionary professors opposed on the grounds that he was a Pole. Mechnikov would not tolerate the idea of determining the value of a scientist on the basis of his nationality. Much later, when Mechnikov lived abroad, he disapproved of German scientists' chauvinist attacks on Bordet, a Belgian. In his *Immunity in Infectious Diseases,* Mechnikov wrote: "It is a grave mistake to adopt a nationalistic point of view in scientific problems." (Footnote on p. 455.)

* * *

A severe and impartial judge in matters scientific, and relating to social duty, Mechnikov was exceptionally kind, cordial and attentive to those around him. His care and solicitude for his friends knew no bounds and gave rise to numerous nicknames, slightly ironical but always good-natured and respectful. For instance, his friends called him "Mama Mechnikov," and I. Sechenov always addressed him in his letters as "My dearest Mama." The young scientists at the Pasteur Institute referred to him as *Père Metsch,* the children living in the vicinity of the institute knew him as Father Christmas, because his pockets were always filled with sweets for his little friends.

His appearance, too, was unusual. In his recollections, Bezredka said: "Those who have seen Mechnikov well remember this striking man, one of the most popular in Paris, his extraordinary appearance which became a byword, his heavy tread bespeaking an unbending will, his eyes, kind and sparkling behind his glasses, his accessibility and invariable kindness."

CONCLUSION

Many and varied are the services Mechnikov rendered science, humanity and his country. Briefly, they are as follows:

In biology Mechnikov discovered a number of new animal groups, established genetic relationships among seemingly distant representatives of the animal kingdom, clarified numerous important details (such as the method of feeding, the nature of reproduction, etc.) in the physiology of lower organisms. His work in embryology is particularly important, since in this sphere, he, jointly with Kovalevsky, created a new branch—evolutionary embryology. To all his work in zoology he applied a single biological and historical method of research. Mechnikov's parenchymella theory provides a highly feasible explanation of such fundamental physiological phenomena underlying the progressive evolution of animals as the appearance of multicellular organisms and of tissues. All his theoretical ideas in embryology and general biology are based on physiology. In particular, he provided proof of the leading role of intracellular digestion in animal evolution. In attributing decisive importance to feeding in the process of evolution, Mechnikov regarded this process as a result of formative influences in environmental conditions. Here, as well as in the solution of other problems (e.g., the explanation of hereditary changes of micro-organisms occurring under the influence of external factors), Mechnikov proved to be a true Darwinist, capable

of assimilating this teaching creatively. He has a perfect right to be considered a pioneer of Darwinism in Russia.

Mechnikov approached medical problems from the standpoint of the evolutionary doctrine, he threw new light on a number of important pathological processes, was the first to give a biological interpretation to inflammation, created the cellular theory of immunity showing the decisive part played by phagocytosis in the organism's defensive reactions. In this work, as well as in his zoological research, Mechnikov remained an evolutionary biologist. Profound erudition and penetration into the essence of the object of his studies enabled Mechnikov to achieve major successes in immunology that constituted a new branch of knowledge for him. According to Mechnikov, immunity in infectious diseases is a particular aspect of the complex and varied reaction constituting the organism's response to the presence of extraneous, primarily protein, substances.

The realization of the immense physiological importance of phagocytosis prompted Mechnikov to study experimentally the vital process of ageing, and, although much in his theoretical premises in this field should be revised, his great service lies in his being the first to call the attention of scientists to combating premature ageing and death, which he did with his wonted ardour and enthusiasm. On the other hand, his work in pathology brought Mechnikov to microbiology and he enriched this branch of science with substantial work on the epidemiology of plague, cholera, typhoid, tuberculosis and syphilis.

This is what N. Gamaleya said of Mechnikov's contribution to medicine: "Decades will pass and men will conquer cancer, leprosy and many other diseases which now are considered incurable. And people will always remember with gratitude the hallowed name of Ilya Mechnikov, the great Russian naturalist who so brilliantly began the campaign for human health."

We have confined ourselves to regarding only the most important aspects of Mechnikov's work, of necessity setting aside a multitude of important problems of descriptive zoology, parasitology, entomology and anthropology to which this extremely versatile biologist gave his attention. Throughout his career, Mechnikov gave utterance to his ideas about the antagonism of microbes, the defensive system of macrophages, cellular poisons—ideas that have been tackled only in our time and have already yielded encouraging results. His brilliant thoughts, his ability to expound, in passing, ideas, which were later verified, is another manifestation of the genius of this great Russian biologist. As Bezredka wrote in 1926: "Ten years have passed since Mechnikov's death. Looking back at his legacy, one cannot help experiencing a feeling of awe at his powerful mind and intuition. Whatever branch of science he approached, whether embryology, general pathology, experimental medicine or even pure philosophy, to each of them he contributed vital ideas, something original and fruitful. Phenomena that no one had been able to explain revealed their essence to him, as if unable to withstand his searching glance.

"His works conceived and performed forty and fifty years ago have preserved their freshness to this day." (*Priroda*, No. 8, 1926.)

Now, more than thirty years after these words were written and a little less than fifty after Mechnikov's death, the most varied branches of biology and medicine are still drawing on the inexhaustible fund of his works, and will do so for many years to come. That is true immortality.

* * *

Science is indebted to Mechnikov for founding a school of research workers, since almost all Russian and many foreign microbiologists and pathologists were his pupils. Heading scientific departments, laboratories and institutes, they established a new trend in science which

developed and ensured Russian microbiology and pathology a place of honour in world science. Mechnikov's pupils have in turn educated hundreds of talented scientists, "spiritual grandchildren" of Mechnikov. It is no exaggeration to say that he is the founder of Russian medical and biological science.

* * *

But Mechnikov's role in modern science is not confined to his influence on his pupils and his pupils' pupils who constitute the majority of Soviet microbiologists and pathologists. Still more important is the fact that biology and medicine in the Soviet Union are still occupied with solving problems which were first posed by Mechnikov. We have had occasion to mention the influence Mechnikov's theory of the origin of multicellular animals exercised on the theoretical work of the outstanding biologists A. Zavarzin and A. Zakhvatkin. His views on theoretical medicine, particularly those concerning the macrophage defensive system, have undoubtedly influenced the medical scientists A. Bogomolets and N. Anichkov.

The work of Soviet microbiologist and cytologist M. Pokrovskaya is an example of the further development of Mechnikov's ideas. He has repeatedly pointed out that the behaviour of the phagocytic elements gives a true picture of the reactivity of the organism, of the state of its defensive forces. The activity of phagocytes in devouring bacteria or necrotic clusters is intimately connected with the production of substances which destroy toxins or render them harmless. When there are no phagocytes or when they are passive, it means that the organism is unreactive, that its ability to protect itself has been lowered. Bearing this in mind, Pokrovskaya has proposed a cytological method to determine the reactivity of the organism and the state of its defensive forces. This method has yielded interesting data concerning the dynamics of the healing of wounds, the course of infectious diseases and the development of immunity. From easily obtained preparations—imprints of tissues—one can determine the quantity and state of various cells, particularly the different macrophages in a given section of the body. This cytological analysis reveals the immunobiological condition of the body and makes it possible to take special measures to strengthen its defensive forces.

A very important behest left by Mechnikov is the maintenance of close contact between biology and medicine and the adherence to the evolutionary and historical method in the solution of both medical and biological problems. In his obituary for Mechnikov, Academician V. Zalensky, a noted zoologist, wrote about his departed friend: "Through his scientific work, Mechnikov has proved the importance of studying the animal kingdom at large in order to solve the general problems of pathology and experimental scientific medicine. What weighty results can be obtained by the experimenting pathologist when he does not confine his research to vertebrates alone!"

A number of works are in progress in the U.S.S.R. precisely in this vein. By way of example, we may mention B. Avetikyan's *Immunological Reactions in Invertebrates and Poikilothermal Animals* dealing with the evolution of the mechanism of antibodies in its historical aspect.

B. Tokin, in his *Immunity in Embryos* (1955), notes an intimate connection existing between embryology and immunology and points out the necessity of studying not only the historical development (phylogenesis) of the main immuno-biological reactions but also their evaluation in the process of individual development (ontogenesis): the appearance and characteristics of the inflammatory reaction in the embryo, its connection with the morphological processes occurring parallel to it, etc.

Further work in this field will doubtlessly bring results important to both immunology and embryology.

Mechnikov's ideas are contained, in one form or another, in the works of many Soviet and foreign embryologists, pathologists and especially microbiologists, all of whom should be regarded as his heirs. And yet the great scientist's legacy has not been utilized to the full; Soviet science must make more extensive and better use of his ideas than has been the case hitherto.

* * *

All his life Mechnikov remained true to the ideals of the sixties: to carry knowledge to the people, to enlighten them and to fight ignorance with the weapon of science. Mechnikov was the author of dozens of popular books about the history of science, its creators and martyrs, the fundamental laws governing the life of the human organism, the major problems of biology, etc. He delivered an immense number of popular reports and lectures for the general public, to say nothing of his series of lectures for students and physicians. Along with Timiryazev and Sechenov, Mechnikov laid the cornerstone for the work of popularizing science, which to this day is the sacred duty of Soviet intellectuals.

* * *

Mechnikov was a great teacher of life. His philosophical treatises, *The Nature of Man, Studies in Optimism, Forty Years' Search for a Rational Outlook,* were permeated with optimism. His ability to make life easier was keenly felt by his contemporaries, as can be seen from Maxim Gorky's letter to K. Timiryazev on the occasion of Mechnikov's death: "It is you and you alone who can and must, with all due simplicity and forcefulness, tell the Russian public how much it has lost by the death of this man, about his precious optimism, about his profound understanding of the value of life and his fight for it." (July 2 [16], 1916.)

Mechnikov's services to science were appreciated in his lifetime. In his report "The Feast of Russian Science," which Timiryazev delivered at the Ninth Congress of Russian Naturalists and Physicians in Moscow in 1894, he mentioned Mechnikov as one of the galaxy of great names constituting the pride of Russian science: "Lobachevsky, Zinin, Tsenkovsky, Butlerov, Pirogov, Botkin, Mendeleyev, Sechenov, Stoletov, Kovalevsky and Mechnikov—these are the Russian people who have glorified the name of Russian in the sphere of thought far beyond the borders of Russia." (*Collected Works*, Vol. IV, p. 41.)

Today, 112 years after Mechnikov's birth and more than forty years after his death, we feel him to be a part of our era. A great optimist and humanist, a devoted lover of science, a champion in the fight against disease, a passionate advocate of truth, Mechnikov lives in our hearts, the model of a scientist, citizen, and man. Not only thousands of Soviet scientists, the pupils and followers of Mechnikov, but the Soviet people, many million strong, know and honour the name of this great scientist and loyal son of his country.

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